Test Definition: SCHPV

Human Papillomavirus (HPV) Detection and High-Risk Genotyping, Self-Collect, PCR, Vaginal

Overview

Useful For

Human papillomavirus (HPV) screening for average-risk, asymptomatic individuals who are eligible for primary HPV testing, have barriers to a speculum exam for a clinician-collected cervical sample for screening, and who are able to self-collect a vaginal sample in a healthcare setting

This test is **not intended for** symptomatic patients (eg, pelvic pain, abnormal uterine bleeding).

Special Instructions

- Evalyn Brush Instructions for Use

Method Name

Real-Time Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is intended for patient collection of vaginal specimens in a clinic/healthcare setting.

For clinician collected cervical specimens, order HPV / Human Papillomavirus (HPV) DNA Detection with Genotyping, High-Risk Types by PCR, ThinPrep, Varies.

For clinical collected vaginal specimens, order VHPV / Human Papillomavirus (HPV) Vaginal Detection with Genotyping for High-Risk Types by PCR.

Necessary Information

Specimen source is required.

Specimen Required

Patient Preparation: For 24 hours prior to specimen self-collection, patients **should avoid** using feminine hygiene products.
Supplies: Evalyn Brush (T990)

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Specimen Type: Vaginal
Collection Container/Tube: Evalyn Brush
Submission Container/Tube: ThinPrep/PreservCyt solution vial
Specimen Volume: 3 mL of solution in ThinPrep/PreservCyt vial
Specimen Stability Information:
Evalyn Brush: Ambient 72 hours
ThinPrep/PreservCyt Vial: Ambient (preferred) 42 days/Refrigerated 42 days
Collection Instructions:
1**. Specimen must be collected by the patient in a healthcare setting.**
2. Provide patient with a labeled Evalyn brush and the accompanying self-collection instruction pamphlet.
3. Following patient self-collection, ensure that the Evalyn brush is tightly capped and appropriately labeled.
4. Place labeled Evalyn brush in a biosafety bag and send to the laboratory.
5. Perform the following steps prior to shipment to Mayo Clinic Laboratories:
a. Label PreservCyt (ThinPrep) vial with appropriate patient information.
b. Uncap PreservCyt vial. Remove pink cap from Evalyn brush.
c. Depress the pink plunger on the Evalyn brush to expose the brush (white bristles).
d. Vigorously plunge the brush, smashing the white brush against the bottom and interior wall of the vial 10 times to maximize sample release. Be careful not to splash.
e. Discard Evalyn brush
f. Tightly recap the PreservCyt vial.
g. Submit the PreservCyt vial for testing.

Specimen Minimum Volume

1 mL

Reject Due To

Uncapped Evalyn brush (no pink cap) Specimen containing CytoRich Red preservative fluid Broken Evalyn brush	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

Persistent infection with human papillomavirus (HPV) is the principal cause of cervical cancer. The presence of HPV has been implicated in more than 99% of cervical cancers worldwide, including both cervical squamous cell carcinoma and cervical adenocarcinoma. Before development of invasive cancer, HPV infects the squamous mucosa cells and/or the glandular cells of the endocervix, leading to clonal expansion and morphologic changes. While the HPV-infected cells are restricted to their normal anatomic location, these changes are classified as cervical intraepithelial neoplasia (CIN). The severity of the morphologic changes and the degree to which those changes resemble the morphology of an invasive carcinoma are used to "grade" CIN. In general, high-grade CIN more closely resembles invasive carcinoma morphologically. HPV can also infect other mucosal cells in the anogenital region, such as the vaginal mucosa, leading to the development of HPV-associated intraepithelial neoplasia as well as invasive carcinoma not involving the cervix itself, although this is less common.

Human papillomavirus is a small, nonenveloped, double-stranded DNA virus, with a genome of approximately 8000 nucleotides. There are more than 118 different types of HPV and approximately 40 different HPVs can infect the human anogenital mucosa. Only a very small percentage of patients who are exposed to HPV will develop CIN. Of those patients who develop CIN, only a small percentage will progress to invasive cervical cancer. Sexually transmission of 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 long-term health consequences. Both high-risk HPV genotypes (especially HPV-16 and 18), as well as persistent HPV infection (eg, an infection that is not cleared by the patient's immune system over time), are associated with an increased chance of progressing to high-grade CIN and invasive cancer.

Data suggest that certain HPV genotypes (eg, HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) are 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.

In developed countries with cervical cancer screening programs, the Papanicolaou test (ie, Pap smear) has been used since the mid-1950s as the primary tool to morphologically detect CIN, the precursor to cervical cancer. Pap smear screening has decreased death rates due to cervical cancer dramatically, since in many cases CIN can be treated and eliminated (eg, by local excision) before it progresses to invasive carcinoma. Although Pap smears and other liquid-based cytology methods have many advantages, they also have limitations: they require subjective interpretation by a highly trained cytopathologist and misinterpretation can occur, morphologic changes that resemble HPV-associated CIN can be caused by other conditions (eg, inflammation), and Pap smear does not sample every cell within the cervix/anogenital region potentially leading to falsely negative results. Perhaps most importantly, Pap smear does not differentiate between HPV genotypes that are high or low risk for progression to cervical cancer and it does not detect very early infections, which may lack a morphological phenotype.

Nucleic acid (DNA) testing by polymerase chain reaction 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 aged 30 years and older with normal cytology.
2) reduce the need for unnecessary colposcopy and treatment in patients aged 21 and older with cytology results showing atypical squamous cells of undetermined significance.

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% 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. Based in part on these data, the American Society for Colposcopy and Cervical Pathology now recommends that HPV 16/18 genotyping be performed on women who are positive for HR-HPV but negative by routine cytology. Women who are found to be positive for HPV-16 or -18 may be referred to colposcopy, while women who are negative for genotypes 16 and 18 may have repeat cytology and HR-HPV testing in 12 months.

Reference Values

Negative for human papillomavirus (HPV) genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68

Interpretation

HPV 16 Positive:
Human papillomavirus (HPV) 16 DNA detected. Referral for colposcopy indicated.

HPV18 Positive:
HPV18 DNA detected. Referral for colposcopy indicated.

HPV High Risk Other Positive:
HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and/or 68 DNA detected. Additional testing (Pap/cytology or dual stain) on a clinician-collected cervical/endocervical specimen indicated.

HPV 16/18/HRO Negative:
No HPV DNA detected. Repeat cervical cancer screening in 3 years.
When providing management advice, take into consideration past test results as per current American Society for Colposcopy and Cervical Pathology guidelines.

Cautions

Patients should refrain from using feminine hygiene products for approximately 24 hours prior to self-collection of the vaginal brush. Use of carbomer-containing feminine hygiene products has been associated with invalid results by the human papillomavirus (HPV) detection/genotyping assay. Carbomer-containing products include:
-Cardinal Health Lubricating Jelly
-Conceptrol Contraceptive Gel
-DynaLybe Lubricating Jelly
-HR lubricating Jelly

-IsoLove Balancing Gel
-KY Jelly (Physician Formula)
-Labicam anti-fungal
-Lavena Moisturizer
-McKesson Lubricating Jelly
-Medline Lubricating Jelly
-Metronidazole Vaginal Gel
-Monistat 1
-Terrasil Ointment Plus Cleansing Bar
-RepHresh Clean Balance
-RepHresh Vaginal Gel prefilled
-Replens Long-Lasting Vaginal Moisturizer
-Surgilube Surgical Lubricating Jelly
-Vagisil anti-itch cream
-Vagisil creme regular strength
-Vagisil ProHydrate
-Vagisil Sensitive Cream
-VCF Contraceptive Foam
-Walgreens Clotrimazole 3
-Walgreens Clotrimazole Vaginal Cream

The vaginal HPV self-collection should not be ordered if active menstrual bleeding or vaginal product use has occurred within 2 days.

Positive HPV results (about 1 in 10) will require a follow-up visit with a speculum exam. Patient should be counseled about that and agreeable to follow-up appointment if needed.

The cobas HPV test is US Food and Drug Administration (FDA)-approved for clinician-collected cervical and endocervical samples in PreservCyt (ThinPrep) media and for patient-collected vaginal samples using an Evalyn Brush in ThinPrep media.

The cobas HPV test detects DNA from high-risk genotypes 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.

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 squamous 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.

Human beta-globin amplification and detection is included in cobas HPV to differentiate HPV negative specimens from those that do not exhibit HPV signal due to insufficient cell mass in the specimen. All HPV negative specimens must have a valid beta-globin signal within a pre-defined range to be identified as valid negatives.

The cobas HPV test performance has not been validated with PreservCyt specimens that have been filled past the maximum fill line of the primary vial. ThinPrep vials that have had any additional PreservCyt fluid volume added or any dissimilar fluid volume added to the initial specimen should not be submitted for testing.

The presence of polymerase chain reaction inhibitors may cause false-negative or invalid results.

Human papillomavirus negative cancers of the cervix do occur in rare circumstances. Also, no cancer screening test is 100% sensitive. Use of this device for primary cervical cancer screening should be undertaken after carefully considering the performance characteristics put forth in the cobas HPV test label, as well as recommendations of professional guidelines.

The use of this test has not been evaluated for the management of women with prior ablative or excisional therapy, hysterectomy, who are pregnant or who have other risk factors (eg, HIV-positive, immunocompromised).

The effects of other potential variables (eg, vaginal discharge, use of tampons, and douching) and specimen collection variables have not been evaluated.

Clinical Reference

1. US Preventive Services Task Force, Curry SJ, Krist AH, et al. Screening for Cervical Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2018;320(7):674-686. doi:10.1001/jama.2018.10897
2. Poljak M, Ostrbenk Valencak A, Cuschieri K, Bohinc KB, Arbyn M. 2023 Global inventory of commercial molecular tests for human papillomaviruses (HPV). J Clin Virol. 2024;172:1105671
3. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP Risk-Based Management Consensus Guidelines for abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis. 2020;24(2):102-131. doi:10.1097/LGT.0000000000000525

Performance

Method Description

The cobas HPV (human papillomavirus) test is a qualitative real-time polymerase chain reaction (PCR) test that detects 14 high-risk HPV genotypes. The test uses primers to define a sequence of approximately 200 nucleotides within the polymorphic L1 region of the HPV genome. A pool of HPV primers present in the Master Mix is designed to amplify HPV DNA from 14 high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). An additional primer pair targets the human beta-globin gene (330 base pair amplicon) as an internal control to monitor the entire sample preparation and PCR amplification process. Fluorescent oligonucleotide probes bind to polymorphic regions within the sequence defined by these primers. The test utilizes a low titer positive and a negative control.(Package insert: cobas HPV:

Qualitative nucleic acid test for the cobas 6800/8800 Systems. Roche Diagnostics; Rev. 2.0, 03/2021)

PDF Report
No

Day(s) Performed
Monday through Saturday

Report Available
3 to 6 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
87626

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SCHPV	HPV Detect/Geno SelfCollect, Vagina	77378-8

Result ID	Test Result Name	Result LOINC® Value
621928	HPV High Risk type 16, PCR	61372-9
621929	HPV High Risk type 18, PCR	61373-7
621930	HPV other High Risk types, PCR	77375-4