A real-time PCR assay that detects 14 high-risk HPV types for the cervical cancer screening

Anyplex™ II HPV HR Detection

14 high-risk HPV types : 16, 18, 31, 33, 35, 39, 45 ,51, 52, 56, 58, 59, 66, 68

Seegene

CE-IVD Marked

Anyplex™ II HPV HR Detection

Human papillomavirus (HPV) has been known as the leading cause of cervical cancer, and HPV types are classified as high-risk or low-risk genotypes based on the association with cervical cancer. HPV16 and 18 specifically are the major high-risk HPV types that are detected in 70% of cervical cancer patients with minor variations in percentage among continents. Therefore, using HPV DNA test in routine screening could help prevent the progression to cervical cancer and could be useful for diagnosis and prognosis of patients.

Anyplex™ II HPV HR Detection kit is a high multiplex real-time PCR product that could provide semi-quantitative information for each of the 14 identified high-risk HPV genotypes. It is suitable for more effective screening in terms of preventing and managing cervical cancer. Also, it provides convenience to users through a streamlined automation system. The application of endogenous internal control that can confirm the entire testing process from sample collection to result analysis helps provide highly reliable and reproducible results.

Key features

Simultaneous detection of 14 high-risk HPV types with a single test

Reliable results by applying endogenous internal control

Improved patient convenience with application of self-collected samples

Provide semi-quantitative information

Analytes

14 high-risk HPV types
16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

Specimens[1)]

Cervical swab specimen
Liquid-based cytology specimen
(ThinPrep® / SurePath™)
Self-collected vaginal specimen

Compatible instrument

Automated extraction & PCR setup
Seegene STARlet

Automated Pre-analytic System
VCMS (Vial Cap Management System)

Real-time PCR
CFX96™ Dx

Trends in diagnosis

HPV DNA test method in becoming more important in cervical cancer screening

- DNA testing is being recommended in 'Guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention' published by WHO in 2021.[1)]
- In the general population, periodic HPV DNA testing is recommended starting from age of 30.

1) WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention. 2nd ed. Geneva: World Health Organization; 2021.

The performance of Anyplex™ II HPV HR Detection kit is validated by fulfilling the international guidelines for cervical cancer screening

Provides reliable test results with validated performance

· It showed equivalent clinical sensitivity, specificity, and reproducibility compared to GP5+/6+—PCR and validated excellent performance in multiple studies. [2), 3)]

International validation criteria

1. Sensitivity and specificity equivalent to ≥CIN2 and <CIN2 detection respectively compared to reference assays
2. High intra- and inter-lab reproducibility unaffected by a clinician

	Reference test (GP5+/6+—PCR)	Anyplex™ II HPV HR Detection	Meets international guidelines
Clinical sensitivity 60 samples with ≥CIN 2	98.3% (59/60)	98.3% (59/60)	○
Clinical specificity 816 samples with <CIN 2	94.1% (768/816)	93.6% (764/816)	○
Intra-laboratory reproducibility	-	96.0% (95% CI=94.3-97.4, n=505)	○
Inter-laboratory agreement	-	96.8% (95% CI=95.3-98.1, n=505)	○

Evaluated HPV assay	Relative sensitivity	Relative specificity	Non-inferiority test *p* value of sensitivity	Non-inferiority test *p* value of specificity	Study
Anyplex™ II HPV HR Detection kit	1.00 1.06 1.01	0.99 1.00 1.01	0.0052 0.0067 0.001	0.0232 0.0354 <0.0001	Hesselink et al., 2016 Jung et al., 2016 Ostrbenk et al., 2018
cobas® HPV (cobas® 4800)	0.98 1.00 1.00	1.00 1.01 1.02	0.0216 0.0093 0.0006	0.0009 0.0012 <0.0001	Heideman et al., 2011 Lloveras et al., 2013 Ejegod et al., 2020
cobas® HPV (cobas® 6800)	0.98 0.98	0.98 0.99	0.0157 0.0157	0.0442 0.0056	Saville et al., 2019 Frayle et al., 2019
Xpert HPV	1.00	1.00	0.0171	0.0269	Cuschieri et al., 2016
RealTi*me* High-Risk HPV	0.99 1.03 0.97	1.00 1.02 1.00	0.0040 0.0112 0.0278	0.0087 <0.0001 0.0003	Carozzi et al., 2011 Poljak et al., 2011 Hesselink et al., 2013
Onclarity™	0.99 0.98 1.02 1.00	0.99 1.00 0.99 1.04	0.0009 0.0245 0.0002 <0.0001	0.0216 0.0155 0.0970 <0.0001	Ejegod et al., 2014 Cuschieri et al., 2015 Ejegod et al., 2016 Bonde et al., 2019

2) Hesselink AT et al., Clinical validation of Anyplex™ II HPV HR Detection kit according to the guidelines for HPV test requirements for cervical cancer screening. J Clin Virol. 2016 Mar;76:36–9.
3) Arbyn M et al., 2020 list of human papillomavirus assays suitable for primary cervical cancer screening. Clin Microbiol Infect. 2021 Aug;27(8):1083–1095.

Testing process

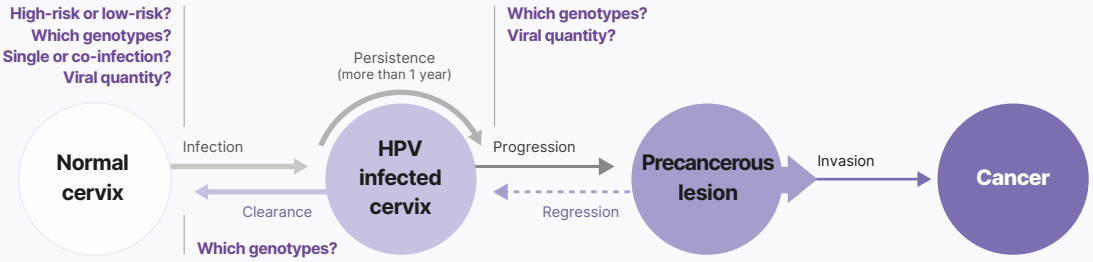
· Improves workflow efficiency through automated testing with one streamlined automation system.

Automated extraction & PCR Setup **Seegene STARlet with VCMS** › Real-time PCR **CFX96™ Dx** › Automated interpretation **Seegene Viewer** + Web-based statistical data analysis **SG STATS**

Purpose of HPV DNA test

· HPV DNA tests should provide maximum information (genotype, co-infection, quantitative result) about the infection to facilitate the clinical follow-up of the patient.

Natural history of cervical cancer[4)]

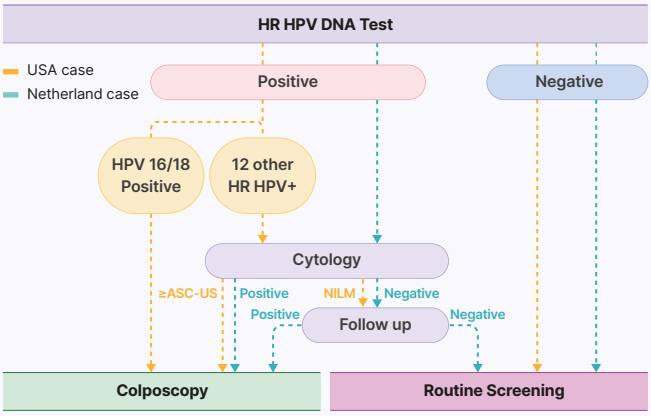


4) Shiffman et al. (2005). *N Engl J Med., 353*(20), 2101-4.

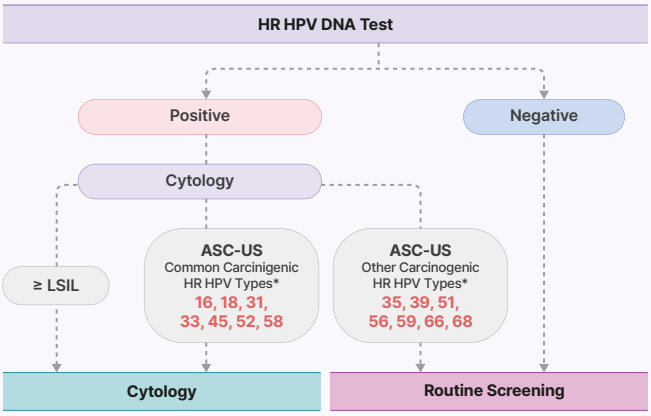
Optimizing HPV-based primary screening program

· General primary HPV screening with cytology triage vs. Alternative triage based on the HPV types.

General HPV Screening Programs[5)]



Alternative Scenario with HR HPV Genotyping



* HPV 16, 18, 45, 31, 33, 52, and 58 account for approximately 90% of the squamous cell carcinomas which are positive for HPV DNA.[6)]

General example of triage algorithmfor primary HPV screening[5)]

1. HPV genotyping for HPV 16, HPV 18 and cytology in US.
2. HPV positive and cytology in Netherland: Women with ASC-US or higher are referred to colposcopy.

A new screening approach is required[5)]

1. **Vaccination effect**: An increase of HPV vaccination coverage is likely to lead to lower prevalence.
2. **Low specificity**: Referring HPV+ women with ASC-US to colposcopy is not efficient, because the large number of women do not have precancer or anything related to cervical cancer.
3. **Management trend**: Risk thresholds rather than individual results.

5) Wentzensen et al. (2016) *J Clin Virol.*,S49-S55
6) WHO. (2017) WHO HPV vaccines: WHO position paper, 244

For primary HPV screening, Anyplex™ II HPV HR Detection kit can help

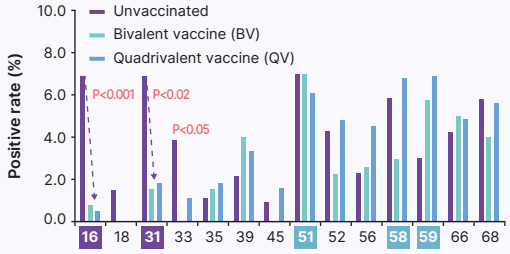
· Setting risk threshold · Considering new alternative scenario · Proposing better algorithm

Through identifying major high-risk HPV types related to approximately 90% of the squamous cell carcinomas.

Effective tool for national cervical cancer screening in post-vaccination era

· The HPV vaccination had a substantial impact on genotype distribution.

1. Monitoring infection dynamics such as type replacement or unmasking in a vaccinated population[7)]



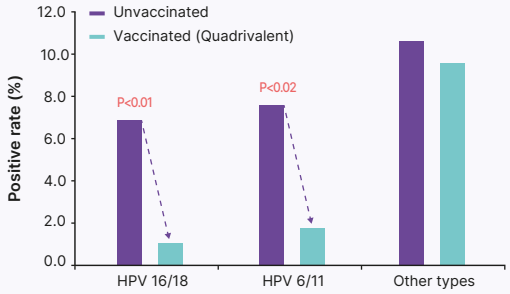
18-29 Yrs women (participant no.: 401)	Unvaccinated	Vaccinated
HPV positive rate	53.5%	46.4%
		42% (BV), 49% (QV)
Most prevalent type	16, 31, 51	51, 58, 59

Study 1. HPV prevalence and vaccine efficacy for 8 years following the implementation of the vaccination program in Luxembourg.

The overall prevalence of HPV showed a very similar rate between the two groups, however, the type distribution was dramatically changed in certain types covered by HPV vaccine and other types assuming cross-protection. For instance, HPV 16, 31, and 33 were significantly decreased in vaccinated women, but not in the unvaccinated group.
Instead, other types such as HPV 51, 58, and 59 were found as the most frequent types in vaccinated women.

7) Latsuzbaia et al. (2019). *Cancer Epidemiol., 63*, 101593.

2. Measuring the efficacy affecting the vaccine policies and strategies[8)]



18-31 Yrs women (participant no.: 409)	Unvaccinated	Vaccinated
HPV 16/18 positive rate	7.5%	1.1%
HPV 6/11 positive rate	8.3%	2.1%
Other HR-HPV prevalent type	11.2%	10.3%

Study 2. Prevalence of vaccine-type HPV in vaccinated and non-vaccinated women in Switzerland.

The prevalence of four types, HPV 6/11 and HPV 16/18, covered by the quadrivalent vaccine was significantly lower in vaccinated women, whereas cross-protection was not observed in this study.

8) Jeannot et al. (2018). *Int J Environ Res Public Health, 15*(7), 1447.

The impact of Seegene's HPV assay in the post-vaccination era

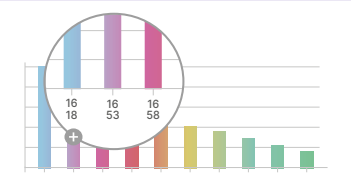
· Monitoring changes of HPV types in a vaccinated population

· Evaluating the prevalence of HPV vaccine types

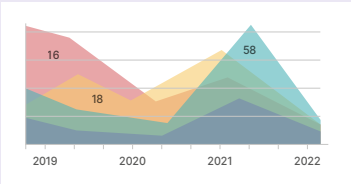
· Measuring the efficacy and cross-protection of vaccine

SG STATS

Seegene's IT solution provides comprehensive information with analysis and visualization



• Example of genotype distribution and co-infection patterns



• Example of yearly HPV infection patterns

SG STATS is accessible to Seegene customers at no additional cost.
To find more information on SG STATS, please contact the sales representative for registration.

Ordering information

Product	Volume	Cat. No.
Anyplex™ II HPV HR Detection	25 rxns	HP10380Z
	100 rxns	HP7E00X

Extraction kit	Cat. No.
VCMS (Vial Cap Management System)	6600532-01

Instrument	Cat. No.
Seegene STARlet	67930-03

www.seegene.com

Seegene

Seegene Inc.
Seoul, Republic of Korea
Tel : +82-2-2240-4000
E-mail : info@seegene.com

Brazil
Belo Horizonte, Brazil
Tel : +55-31-25153003
E-mail : contato@seegenebrazil.com.br

Canada
Toronto, Canada
Tel : +1-800-964-5680
E-mail : canada@seegene.com

Colombia
Bogotá D.C, Colombia
Tel : +57-315-7920200
E-mail : jlrodriguez@seegene.com

Germany
Düsseldorf, Germany
Tel : +49-211-83831-600
E-mail : sgg@seegene.com

Italy
Genova, Italy
Tel : +39-010-667-1796
E-mail : info@arrowdiagnostics.it

Mexico
México city, México
Tel : +52-55-8848-9646
E-mail : mexico@seegene.com

Middle East
Dubai, UAE
Tel : +971-4-558-7110
E-mail : sgme@seegene.com

USA
California, USA
Tel : +1-925-448-8172
E-mail : info@seegenetech.com

HP7E-EN230220B-01