ULISSE BioMed

We build using DNA: the molecule of life

Sagitta™

HPV Selfy HR

Screening of 14 high-risk HPVs with genotypes by real-time PCR

14 High-risk HPV genotypes:

16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

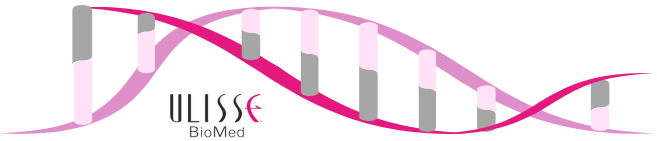
Validated on self-collected samples according to VALHUDES protocol

Validated for primary screening purposes according to Meijer guidelines

CE-IVD Marked

HIGH SENSITIVITY & SPECIFICITY

Multiplex real-time PCR with high sensitivity and specificity by **utilization of SAGITTA™ patented technology**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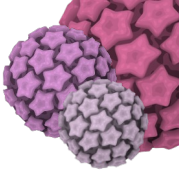


What is HPV?

The Human Papillomavirus, also known as HPV, is the most common sexually transmitted infection affecting millions worldwide. In fact, at least 4 out of 5 women will have been infected with the HPV virus by age 50.

There are over 120 known types of HPV; approximately 40 of these types infect the epithelial lining of the anogenital tract, mouth, and throat. In the majority of individuals (about 90%), HPV infections are asymptomatic and usually clear up within 2 years without the need for any medical intervention. However, a small proportion of infections from any of the 14 high-risk HPV types can persist and progress into cervical cancer. These 14 high-risk types alone account for nearly all cervical cancer cases and therefore early detection of HPV infection is critical in order to prevent cervical cancer.

HPV and Cervical Carcinoma

After breast cancer, cervical cancer is the second most common cancer in women.

Unlike all other types of cancers, cervical carcinoma has a clearly defined causation: persistent infection with one of 14 high-risk HPV subtypes. In fact, over 99.7% of cervical cancer arises from persistent HPV infection, with HPV 16 and 18 alone accounting for over 70% of cervical cancer cases.

HPV has been identified as the leading cause of cervical cancer in women as well as a growing risk factor in oropharyngeal cancer. Although over 150 related HPV strains have been identified, only a subset of whole HPV was identified as major risk factors for cervical cancer. While HPV16 and HPV18 have clearly been implicated as causative agents, the influence of other high-risk HPV genotypes on the severity and progression of cervical cancer have been reported.

The importance of genotyping

Beside the HPV infection, the co-infection of high-risk HPV strains has now been identified as risk factors for increased co-morbidity and disease progression. Outcome-based clinical studies regarding HPV vaccines have demonstrated the advantages of long-term monitoring of infected HPVs in association with persistent efficacy and cross-genotype protection. Unfortunately, most HPV diagnostic tools are not suitable for the detection, identification and quantitation of multiple HPV genotypes.

SAGITTA™ HPV Selfy HR is specifically designed for simultaneous detection and genotyping of 14 high-risk HPV genotypes, including HPV16 and HPV18, which contributes to cervical cancer, even from self-collected samples. SAGITTA™ HPV Selfy HR is a fast and reliable solution for the detection of HPV infection, providing a much-needed multiplex diagnostic solution to assist in prognosis and long-term patient outcome.

Sagitta®

HPV Selfy HR Kit

Is my patient infected with one of the 14 high-risk HPV genotypes?

Screen your patients for the 14 high risk HPV subtypes.

Which of the 14 high-risk HPV genotypes is my patient infected with?

Specifically detect and simultaneously genotype each of the 14 high-risk HPV subtypes individually for best diagnosis and triage.

The purpose is to continuously monitoring the HPV infection status of your patient, to ensure that the infection of one specific genotype does not persist longer than two years: it is the persistence of one or more HPV genotypes, rather than infection itself, that leads to cervical cancer.

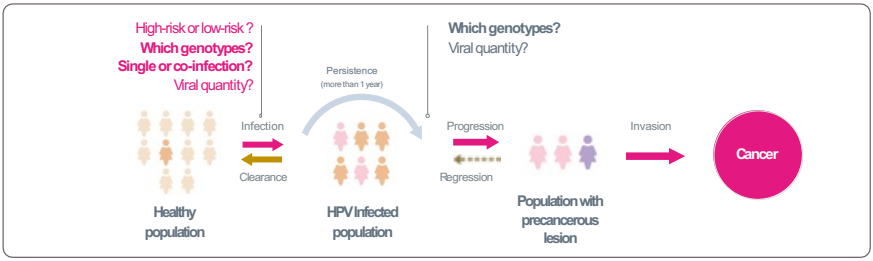
For more information on SAGITTA™ HPV Selfy HR, see page 4.

Cervical cancer is preventable and treatable if identified in earlier stages

HPV DNA Test: a useful source of clinical information

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

Evolution to cervical cancer [1)]



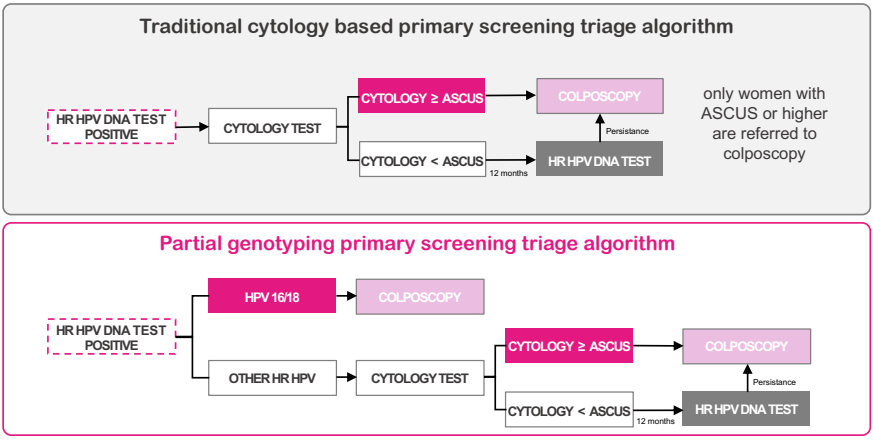
1) Adapted from Shiffman M *et al.* The promise of global cervical cancer prevention. *N Engl J Med* (2005) 353(20) : 2101-4

Current Clinical Guidelines

Based on the World Health Organization (WHO) guidelines, all women over the age of 30 are advised to undergo routine testings for HPV, often at the same time as their regular Pap smear. The changes in the cervix that could lead to cervical cancer may take several years (up to 10 years or more) to develop before becoming detectable by conventional cytology and pathological examination, therefore HPV testing is critical to allow for early detection. The earlier HPV is detected, the more time doctors and patients have to monitor, test, and prevent the eventual development of cervical carcinoma.

The actual general primary HPV screening is essentially based on cytology triage and does not consider useful information that could derive from the genotyping analysis.

PrimaryHPV screening based on cytology triage: traditional vs partial genotyping approaches



Policy has developed to manage HPV16 and HPV18 similarly with immediate colposcopy recommended based on their higher risk for cancer. However, HPV16 is associated with a different spectrum of disease than HPV 18, and optimal management should recognise this. HPV16 is more associated with precursor lesions that can be identified at colposcopy and is the most common type found not only in cancer but also in precursor cervical intraepithelial neoplasia (CIN) grade 2 (CIN2) and CIN3 lesions. In contrast, HPV18 is more often associated with endocervical lesions which are often not visible at colposcopy and thus are often not detected and treated at an early stage.

New scenarios that enhance HPV types relevance

Risks associated with other HPV types vary further by genotype, and ideally could be subject to differential type-specific management. In terms of clinical management, the key factor in determining risk is the positive predictive value (PPV), either for CIN2+ or CIN3+, which are much more likely to progress to cancer. PPV is more important than prevalence for some low prevalence types, notably HPV 33 type, carrying a high PPV for a precursor lesion. Ranking HPV types hierarchically based on maximising the PPV and disregarding co-infections with HPV types higher in the hierarchy has proven useful. Several screening studies have shown HPV16 stands at the top of the hierarchy, followed by HPV33 and HPV31, with HPV18 ranking much lower (Figure 2).

PPV for high-risk HPV types overall and stratified by viral load [2)]

HPV Type	PPV (%) by Viral Load (CIN2+)			
	Low	Medium	High	All
16	3,89	6,76	17,64	11,91
33	4,39	9,94	10,56	8,12
31	4,01	8,90	10,94	6,77
35	3,49	6,00	10,10	5,40
18	2,01	2,83	7,90	5,10
58	1,14	2,11	6,11	3,94
51	2,27	4,38	4,47	3,35
45	1,32	2,35	3,37	2,34
39	1,98	2,77	2,11	2,20
52	0,39	1,15	4,57	2,03
59	0,93	1,09	2,79	1,84
56	0,17	2,42	1,32	1,04
68	1,02	0.00	0,82	0,58

2) Adapted from Adcock R et al. Role of HPV genotype, multiple infections and viral load on high-grade CIN. Cancer Epidemiol Biomarkers Prev. 2019 Nov; 28(11):1816-1824

Color coded for 3 years risk of CIN2+

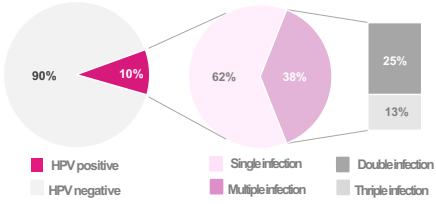
<2%
2-5%
5-10%
>10%

HPV vaccination affects the prevalence of genotypes and the collection of data in different relevant geographies is crucial for the development of correct local screening and triage practices.

Knowledge of HPV genotype is useful in clinical decision-making for management of HPV positive women. HPV16-positive women clearly need the most intensive management, and HPV31/33 positive women probably also need more follow-up than other types. HPV18 remains a challenge and a better way of identifying these lesions is needed. Tracking the persistence of the same HPV type over the time, thanks to single strain genotyping, could help in prevent the development of lesions related with the persistence of a single HPV type.

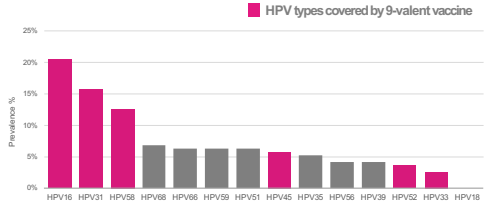
Genotyping is helpful to track and monitor HPV types coinfections. Interest in coinfections has been heightened because of the availability of vaccination against HPV. The introduction of vaccination into a population may modify an established equilibrium in the distribution of HPV types. In addition to immunologic factors involved in the interplay between the types, competition or synergy could exist among HPV types infecting the same epithelium. A conceivable outcome of successful HPV vaccination is that the decreased prevalence and incidence of the HPV types targeted by vaccines would influence the distribution of infection with other HPVs.

Prevalence of multiple infection [3)]



3) Adapted from Avian A et al. (2022) Clinical validation of full genotyping HPV Selfy assay according to the international guidelines for HPV test requirements for cervical cancer screening on clinician-collected and self-collected samples.

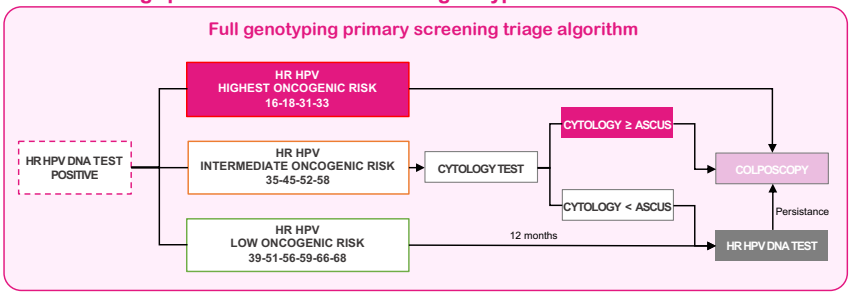
Distribution of high-risk HPV types [3)]



New screening approach is possible

Through identifying major high-risk HPV, including vaccine-covered types, SAGITTA™ HPV Selfy HR could help optimizing HPV-based primary screening program and triage algorithm by: i) setting risk threshold; ii) considering new alternative triage; and iii) proposing better algorithm.

Alternative triage procedure based on the HPV genotype [4)]



4) Adapted from Jesper H. Bonde et al. Clinical Utility of Human Papillomavirus Genotyping in Cervical Cancer Screening: A Systematic Review. 2020 Jan; 24 (1): 1–13.

A new screening approach is required, due to:

1. **Vaccination effect**: an increase of HPV vaccination coverage is likely to leading lower prevalence
2. **Low specificity**: Referring HPV+ women with ASCUS 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

*It depend on many factors including a societal perception of risk, established clinical practice, different weight on benefits and harms, health economic considerations, and health infrastructure.

For primary HPV screening, SAGITTA™ HPV HR can help

1. Setting risk threshold
2. Considering new alternative scenario
3. Proposing better algorithm
4.Monitoring HPV epidemiology in relation with vaccines

through identifying major high-risk HPV, including vaccine-covered types

Our Diagnostic Solution

Sagitta™

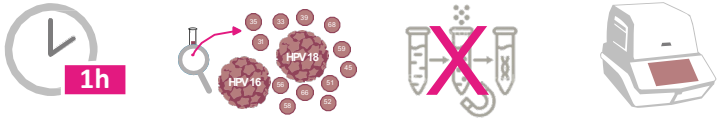
HPV Selfy HR Kit

The first defense against cervical cancer

MADE IN ITALY · REAL TIME PCR · CE IVD Marked

validated with self-collection devices

With HPV Selfy, go **from sample collection to results in one hour**, with no need of extracion and purification of nucleic acids, for a smoother, smarter, and faster healthcare experience for your patients by providing, in the same reaction, an **accurate genotyping of 14 high-risk HPV types**.



Rapid and precise analysis · Native Genotyping · No need for extraction · No custom equipment

Principle behind HPV Selfy Assay

HPV Selfy HR provides a superior clinical response, very specific and sensitive, and a native genotyping capability given to its ability to perform accurate melting curve analysis, even without DNA extraction.
The assay is designed to obtain strain-specific melting curves coupled with amplification curves allowing to generate a unique HPV genotype-specific melting fingerprint profile, thus allowing to obtain genotyping information in the same PCR reaction.
Melting curve analysis is an additional post-PCR step that further characterizes the amplicons by studying thermal denaturation of double-stranded DNA. This method allows to discriminate sequence variations and features among different amplicons, and even single nucleotide polymorphisms (SNPs) can be observed.
Nowadays melting curve analysis requires extremely pure extracted DNA and dedicated chemistry: this so far restricted its application in diagnostic kits. Moreover usage of intercalating dyes affected negatively specificity of the assays, because also aspecific amplicons gain visibility in the amplification curve measurements.
With Sagitta™ technology and UlisseFaster DNA reagents, is finally possible to perform precise Melting Curve analysis even on raw samples, thus possibly escalating melting curve analysis usage in most labs. Moreover, Sagitta™ technology is based on mastered primer design, that allows only extremely specific amplicons to be generated while aspecific signals can be ruled off by the same melting curve analysis.
A user-friendly software interface allows the lab users to obtain full information in a single click in a time-saving manner.

HPV Selfy is the 1st HPV detection + genotyping test, NOT requiring DNA extraction, in a single step reaction, validated also on self-collected samples.

Analytes

- **14 High-risk HPV genotypes :**
  16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68
- Endogenous Control
- Beta Globin

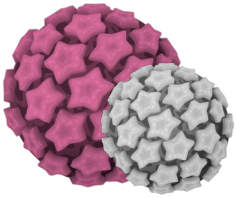
Specimens

- Liquid based cytology specimen (i.e. ThinPrep®)
- Cervical swab
- Vaginal swab (self-collected samples)
- Anal swab
- Urethral swab
- FFPE
- Oropharyngeal swab

Features

- Accurate genotyping of 14 high-risk HPV types in a single reaction
- Multiplex real-time PCR for reliable results by utilization of SAGITTA™ patented technology
- Compliance with guidelines for HPV primary screening
- Compatible with a wide range of real-time PCR devices (Biorad CFX96, Thermo Fisher Quant Studio 5, Agilent Aria)
- Compatible with Ulisse Faster DNA pre-treatment buffer to avoid extraction and purification of nucleic acids
- Amenable to automated sample handling and assay systems
- Endogenous Internal Control for assay validity
- Convenient data interpretation by the HPV Selfy software

Ordering information



Sagitta™

HPV Selfy

Kit Components (for 50 rxns)	Quantity
1 X HPV Mix	0.35 ml
1 X β-globin Mix	0.35 ml
1 X Reaction Mix	1.50 ml
1 X $MgCl_2$ 25 mM Solution	0.10 ml
1 X Positive Control	0.10 ml
1 X Negative Control	0.10 ml

- Single genotyping of 14 HR-HPV subtypes in order to:
  - track persistent infections of HR-HPV types,
  - monitor HR-HPV co-infections,
  - optimise screening and triage practices.
- Multiplex real-time PCR for reliable results by utilization of Sagitta™ patented technology.
- Validated for screening purposes.
- Validated with self-collection devices.
- Validated on several specimens.
- Possibility to avoid nucleic acids extraction and purification using Ulisse Faster DNA.
- Convenient data interpretation by proprietary software.
- High sensitivity and specificity.
- Great value for money.

Product	Package Volume	Cat. No.
Sagitta™ HPV Selfy HR	**50 rxns**	**UBM0013-050**
Sagitta™ HPV Selfy HR	**100 rxns**	**UBM0013-100**
UBM Ulisse Faster DNA (pre-treatment buffer for direct PCR - avoid nucleic acid extraction and purification)	**50 rxns**	**UBM0014**
HPV Self-collection set (Flocked swabs for vaginal mucus self-collection)	**50 pcs**	**UBM0015**
Instrument	**Type**	**Cat. No.**
Agilent | AriaDx Real-Time PCR System	**Real-time PCR thermal cycler and optical reaction module**	**UBM0045**
Bioer | GenePure Pro Nucleic Acid Purification System (NPA32P)	**Fully automatic nucleic acid extraction and purification system | 32 samples**	**UBM0046**
Bioer | MagaBio plus Virus DNA purification kit	**Nucleic acid extraction and purification reagent**	**UBM0047**
Transferpette | Micropipettes set	**Set of 5 air displacement pipettes | 0.5 - 1,000 µl**	**UBM0048**

Not Available for Sale in the United States

Related Products

The **widest product range** for the detection and genotyping of HPV based on real time PCR technology

- **HPV Selfy Extended - 30 HPV types (UBM0025)**
  HPV 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 66, 68, 69, 70, 73, 82
- **HPV Selfy 19 HR (UBM0024)**
  HPV 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 69, 73, 82
- **HPV Selfy 16 HR/LR | 14HR+2LR (UBM0021)**
  HPV 6,11,16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68
- **HPV Selfy 11 LR (UBM0022)**
  HPV 6, 11, 40, 42, 43, 44, 54, 61, 70, 81, 84
- **HPV Selfy - 10 LR/pHR (UBM0020)**
  HPV 6, 11, 26, 42, 53, 69, 73, 81, 82, 84
- **HPV Selfy 5 pHR (UBM0023)**
  HPV 26, 53, 69, 73, 82

Full genotyping of up to 30 HPV types in a single assay!

Who are we?

Ulisse BioMed is an healthcare biotech company listed on the Euronext Growth Milan stock exchange. The company has three proprietary technology platforms capable of generating innovative and competitive products: Sagitta (molecular diagnostics), NanoHybrid (theranostics and diagnostics) and Aptavir (diagnostics). UBM owns a portfolio of intellectual properties made of 8 international patents that cover the three technology platforms (3 related to Sagitta, 2 related to NanoHybrid, 1 related to Aptavir and 2 transversal to the three platforms), two of them are granted in Italy and in Europe.

Who we are

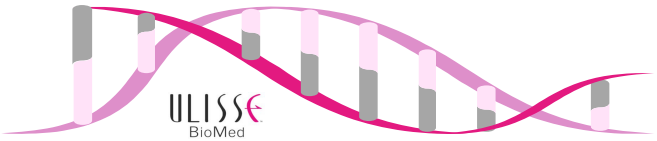
A team of forward-thinking scientists in medical and human genomics with a vision to better healthcare for humanity, one diagnostic solution at a time.

Our goal

To develop diagnostic kits that enable physicians to peer deep into the unique origins of health and disease within their patients and radically customize the healthcare they can deliver. Our goal is to deliver simple and powerful diagnostic solutions that drive healthcare forward.

Early detection of HPV infection is critical for cervical carcinoma prevention and management.

Join us in our movement to diminish the number deaths caused by cervical cancer.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HYPE ON THE GENOTYPE

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