Papillomavirus Infection (HPV)
Reagent Kits Format and Composition

By detection type:

FRT format – real-time fluorescence detection
The format is intended for use of specialized equipment for real-time PCR. Labeling of reagent kits reflects the adapted equipment:
- RG — Rotor-Gene 3000/6000 (Corbett Research)
- IQ — iCycler/iQ5 (BioRad)
- Mx — Mx3000P/Mx3005P (Stratagene)
- SC — SmartCycler (Cepheid)

FEP format – end-point fluorescence detection
The format is intended for amplification in a standard thermal cycler with subsequent detection of the end point fluorescent signal on a specialized fluorescent detector, for example, ALA-1 (BioSan), Jin (DNA-Technology) or a real-time PCR unit with detection of fluorescence end point, for example, Rotor-Gene 6000 (Corbett Research).

EPh format – electrophoretic detection
The format is intended for detection with use of electrophoresis in agarous gel.

By composition:

Complete Set Reagent Kit format
The kit includes reagents for extraction, amplification and detection.

Amplification Reagent Kit (PCR Kit)

By hot start type and filling

“Wax” format
“Hot Start” is ensured by a wax layer:
- The kit includes PCR test tubes ready for use with a lower mixture applied under wax;
- The kit includes vials with reagents not dispensed into PCR test tubes.

“Hot-Start” format
“Hot Start” is ensured by modified polymerase activated at heating (TaqF):
- The kit includes vials with reagents not dispensed into PCR test tubes, modified TaqF polymerase is used.

As compared to PCR test tubes ready for use with a lower mixture applied under wax this format improves the quality of the “hot start” and quality of results without increasing the associated labour intensity. On preparation to PCR test all components are premixed and then the reaction mixture is dispensed into PCR test tubes once.
Human Papillomavirus (HPV)

General Information

Introduction

Human Papillomaviruses (HPV) are a widely spread heterogeneous virus group. HPV have a ring-shaped DNA with a genome containing about 8 thousand pairs of bases. Taxonomically papillomaviruses are divided by kinds (designated by Greek letters (a, b, g etc), types (designated by Arab figures and the letter indicating the kind, e.g. a7, a9, b1 and so on), sorts (designated by Arab figures, e.g. 16, 18, 6, 11 etc.).

Epidemiologically there are cutaneous, troptic to the keratinizing epithelium types (for the most part, kinds b and g), and mucous and anogenital (tropic to mucous tunics) types of the virus (a kind). The latter type includes subgroups of the low (kinds a1, a8, a10) and high carcinogenic risk (kinds a5, a6, a7, a9) depending on their ability or inability to render transforming action on the epithelium cells. Epidemiological studies conducted within the recent years showed that the high carcinogenic risk group includes types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82. Types 26, 53 and 66 belong to the category of the supposedly high risk. The low carcinogenic risk group includes types 6, 11, 40, 42, 43, 44, 54, 61, 72, 81. The remaining types belong to the unidentified risk category and often are not associated with development of pathologies.

Low and high carcinogenic risk HPV can exert productive effect on epithelium cells resulting in development of the classic manifestations of the papilloma-virus infection - pointed condylomas of genital organs (genital condylomas) and light degree dysplasia (L-SIL or CIN1). Types of high oncogenous risk are distinguished by their ability to transform epitheliocytes causing development of precancer (high and medium degree dysplasias, H-SIL or CIN2,3) and cancer. It’s necessary to underline that development of dysplasias is not accompanied by formation of pointed condylomas.

Classification of Human Papillomaviruses

- HPV (more than 100 types)
  - Anogenital (mucosal) More than 30 types
  - Cutaneous. EV and others
    - High Carcinogenic Risk (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82, [26*, 53*, 66*])
    - Low Carcinogenic Risk (5, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81)
    - Transforming effect. Grave degree dysplasia. Carcinoma in situ. Invasive cancer
    - Productive effect. Pointed condylomas of genital organs. Papillomatosis of larynx in children

* Types 26, 53 and 66 belong to the supposedly high carcinogenic risk category.
Strategies of use of HPV tests in diagnostics of cervical pre-cancer and cancer

Screening and observation strategy

- The screening study with the aim to detect persons belonging to the cervical cancer elevated risk development group (infected with high-carcinogenic risk HPV) starting from the age of 25-30 years with the interval 3-5 years.
- A more accurate inspection of the detected persons for presence of pre-cancer and cancer pathology with use of instrumental diagnostics methods.
- Timely treatment of the pre-cancer pathology.
- Meticulous observation of persons from the risk groups but without manifestations of the pre-cancer pathology.

Algorithm of HPV DNA test use combined with cytology on the first screening stage

<table>
<thead>
<tr>
<th>Result of cytology and HPV DNA</th>
<th>Routine screening</th>
<th>HPV (-) Cytology (-)</th>
<th>HPV (+) ASCUS</th>
<th>HPV (+) ASCUS</th>
<th>L-SIL or higher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colposcopy</td>
<td>0-3 months</td>
<td>0-6 months</td>
<td>Repeated cytology, HPV DNA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The algorithm is intended for women older than 30.
Wright T., 2004

Algorithm of HPV DNA test use for resolution of dubious results of the cytological analysis (ASC-US)

<table>
<thead>
<tr>
<th>Not certain cytology result (ASC-US)</th>
<th>HPV DNA test</th>
<th>Negative</th>
<th>Colposcopy/Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine screening</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ASCCP Guidance. Wright TC, 2001

Algorithm of HPV DNA test use as a primary screening method with subsequent cytological examination

<table>
<thead>
<tr>
<th>High Carcinogenic Risk HPV DNA Test</th>
<th>DETECTED</th>
<th>NOT DETECTED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Cuzick, 2003, 2006

High Carcinogenic Risk Human Papillomaviruses (HCR HPV)

A group of high carcinogenic risk types is represented by 15 genotypes the most widely spread among which are ten: 16, 18, 31, 33, 35, 39, 45, 52, 58 and 59. Currently the convincing evidence has been obtained that the HPV acts as a promoter of development of cervical cancer, greater portion of anal cancer (about 90 percent of cases), about 40 percent of all cases of cancer of vagina, vulva, penis, 10-15 percent of cases of the oral cavity and larynx cancer.

High Carcinogenic Risk Human Papillomavirus and Cervical Cancer

Cervical cancer (CC) is one of the most widely spread oncolopathological pathologies that ranks second by the incidence in women in the world. Each year about 600 thousand of new CC cases are registered in the world with more than 250 thousand lethal outcomes. The virus nature of this cancer is confirmed by the World Health Organization. HPV is detected practically in 100 percent of cases of cervical pre-cancer and cancer, detection of HPV on the dysplasia lacking stage is characterized by 3 hundred fold increase of the CC development risk. Owing to the fact that the cervical cancer (CC) has a long development period and a fail-safe recognizable pre-clinic phase there's a possibility to detect and prevent the disease on its early stage. Discovery of the virus nature of cervical cancer and development of HPV tests allowed improvement of the screening system based only on the cytological examination, which increased the sensitivity of the pre-cancer and cervical cancer detection.

Peculiarities of Papillomavirus Infection

Contamination with human papillomavirus has a number of important peculiarities neglect of which makes use of HPV testing associated with a number of difficulties in the results interpretation.

On the one part:

- The majority of contaminated women (about 80 percent) are cured of HPV within 9-15 months from the moment of contamination without therapeutic procedures.
- Infection results in development of pre-cancer in a small part of infected women (about 0.5 percent).
- The average period from contamination to development of cervical pre-cancer and cancer makes about 20 years.
- There are no effective therapeutic methods at the latent infection stage (no changes in the cytological and/or colposcopic pictures, the virus is not detected).

On the other part:

- HPV is a major cause of cervical cancer.
- The incidence of infected women to develop cancer is by 300 times higher as compared to non-infected ones.
- Infection is cunning and very often infected people have no complains associated with it and is not detected at examination till its development to the invasive cancer stage.
- Clinical manifestations of papillomavirus of high carcinogenic risk might be disguised by other diseases of the urogenital tract, which prevents their detection with use of conventional methods.
- Taking into account the listed peculiarities of the papillomavirus infection one can conclude that the positive result of testing for the virus presence amounts to:
  - Classification of a patient to the high risk group by development of cervical cancer;
  - Need in additional meticulous diagnostic procedures for detection of the current stage of the infection, ruling out of grave dysplasia and cervical cancer;
  - Necessity in control of infection in absence of clinical or sub-clinical manifestations.

Negative result of testing is defined as lack of risk of development of grave dysplasia and cancer.
Diagnostics of High Carcinogenic Risk Papillomavirus Infection

The major task of diagnostics of high carcinogenic risk papillomavirus infection is detection of pre-cancer changes. At present detection is achieved through use of cytologic, colposcopic, histologic methods (that detect changes of epithelium characteristic of papillomavirus infection, dysplasia and cancer) and molecular-biological methods allowing detection of contamination and genetic typing of HPV.

Cytologic smear analysis is a method to detect morphological changes of cells, including those related to HPV. The method is not specific for contamination with high carcinogenic risk viruses and detects cases of light dysplasia connected with low carcinogenic HPV. The quality of the result to a significant degree depends on the qualification of the cytologist (as interpretation of results is subjective) and on the selection of the dying method. The most informative dying method is Papanikolaou’s method, the less informative one is Pappenheim and Leischmann’s method, the method with the lowest information value (nevertheless, the method most often used in Russia) - Romanosky-Giems’s method. The sensitivity of the cytological analysis with dying by Papanikolaou’s method as related to grave dysplasia and cancer makes at the average 58 percent (variation from 20 to 87 percent) with specificity - 90-97 percent. The forecasting value of the negative test result is low for patient observation within several years. Owing to this factor the recommended interval of cytological analyses for periodic health examination and screening makes 1-3 years.

Colposcopy is not specific for papillomavirus infection as it detects morphological changes of epithelium in vivo. Due to the fact that it’s a good secondary method of the cervical pathology confirmation attempts to use the colposcopy as a screening test showed that the sensitivity of the examination makes about 75 percent with 20 percent specificity. In addition to this, the method requires time, high qualification of the colposcopist, availability of special equipment in the doctor’s consulting room.

Histological examination is a golden standard of diagnostics but can’t be used as a screening method due to its invasive nature and labour intensity, that’s why it serves as a secondary diagnostics method.

Molecular-Biological Methods

High Risk HPV detection doesn’t allow determination of the infection stage but expressly indicates its presence or absence. Owning to this fact this group of methods can be used only in combination with clinical examination methods. At the same time exact ranging in the high risk group with use of molecular tests allows focusing attention on separate patients and increasing effectiveness of establishment of the infection stage by clinical methods. The experience of Europe and US showed that a combined use of HPV-testing and cytology allows increasing the sensitivity of detection of pre-cancer and cervical cancer to 96-99 percent and increasing the recommended intervals between regular (screening) examinations up to 5-7 years. This is possible as female patients with the negative result to the HPV test (including a group with cytological L-SIL and ASC-US) within 5-7 years do not develop grave degree of dysplasia.

HPV genetic typing gives additional possibilities to determine the forecast of the disease course. The necessity of genetic typing might be justified since:

- Determination of several genotypes of the virus is associated with less favorable forecast of the disease course and a high risk of persistence.
- The carcinogenicity risk of various genotypes of the high risk group is not equal. 16 and 18 types of HPV possess greater carcinogenicity, there are recommendations on determination of these two genotypes of the virus after the test for a wide spectrum of types with a more aggressive tactics of patients’ treatment: determination of 16 and 18 HPV genotypes requires conduction of a colposcopy analysis, detection of other types of high risk carcinogenicity causes the necessity to conduct a cytological analysis and then if the cytological result is positive - to conduct colposcopy.
- Genetic typing allows differentiating re-contamination from the persistent infections at the repeated visit of the patient. It’s necessary to obtain detailed information as the danger lies in the chronic persistent form of infection, whereas recent contamination is most likely to be cured spontaneously. Re-infection is suggested by the change in the genotypes spectrum, persistent infection is determined if the virus genotype is retained within a year after the first analysis, repeated contamination by the same virus genotype after recovery without treatment is practically impossible.

Strategies of HPV-test use for diagnostics of pre-cancer and cervical cancer

Strategy of HPV-test use in monitoring of therapy CIN2+

This strategy supposes double examination: cytology+HPV-test in 6 months after the conducted surgical treatment. If the double negative result is obtained, the female patient is considered completely cured (as opposed to the classical scheme under which it’s necessary to get 4-5 negative cytological conclusions in order to confirm the status of recovery).

Algorithm of HPV DNA test for monitoring of CIN2+ therapy

Use of HPV tests in accordance with the described algorithms, recommended by a number of international organizations as:

- World Health Organization International Agency of Research of Cancer (IARC WHO);
- American Society for Colposcopy and Cervical Pathology (ASCCP);
- European Organization of Gynecological Infections and Neoplasia (EUROGIN);
- European Society of Infectious Diseases in Obstetrics and Gynecology (ESIDOG);
- American College of Obstetrics and Gynecology (ACOG).

Advantages of HPV testing as compared to cytology:

- The diagnostic sensitivity as related to grave dysplasia and cervical cancer (93-99 percent) is significantly higher (for the cytological smear the sensitivity makes 50-60 percent);
- The forecasting value of the negative result is much higher.

ASCCO Guidance, Wright TC, 2001
AmpliSens® Reagent Kits for screening diagnostics

The international experience of HPV-testing application allowed exact requirements to tests for screening diagnostics were formulated. Federal State Scientific Institution Central Scientific and Research Institute of epidemiology of the Federal control service in the sphere of consumer rights and people welfare developed kits of reagents for diagnostics of the papillomavirus infection of the high carcinogenic risk satisfying all the presented requirements:

**HPV-test must detect only types of high carcinogenic risk.** Non-observance of this rule and detection of all HPV genotypes will result in extremely low diagnostic specificity and low information value as similar tests in addition to genotypes of high carcinogenic risk will detect genotypes not responsible for development of pre-cancer and cervical cancer and very often not connected with any pathology of the urogenital tract.

<table>
<thead>
<tr>
<th>HPV incidence at cervical cancer (%)</th>
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<td>HPV types</td>
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<td>- 6, 11</td>
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HPV-test must detect no less than ten genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58), which ensures more than 95-percent diagnostic sensitivity of the test.

The diagram shows a cumulative factor of the incidence of various high risk HPV genotypes in the event of cervical cancer.

As is seen, detection of 2 most widely spread HPV genotypes will have a low diagnostic sensitivity (about 72 percent). Tests detecting a wide range of high risk HPV genotypes will have a high diagnostic sensitivity.

**HPV test must have the possibility to detect** only clinically significant concentration of the virus or differentiate a clinically important from the insignificant one, which considerably affects the specificity of the examination.

The reasons to apply a clinical significance threshold are listed in a number of works stating that the viral load lower than the certain value ("significance value") doesn’t occur in samples of grave dysplasia and cancer and is not associated with the infection regression (clinically insignificant contamination). The load above this threshold is designated as clinically important contamination. The second threshold is identified too ("regression threshold"). The vital load above this value is identified as elevated and is associated with a greater possibility of presence or progression in CIN2,3. On the basis of studies conducted in the Federal State Scientific Institution Central Scientific and Research Institute of epidemiology and world medical literature data the threshold HPV concentrations were determined in the sample: 3 log (or $10^3$) HPV genome per 100 thousand human cells - a clinical significance threshold, 5 logarithms of HPV per 100 thousand cells – a progression threshold. In the course of the validation it was proved that introduction of the clinical significance threshold allows increasing the diagnostic specificity of the study by 20 percent while retaining the diagnostic sensitivity.

**AmpliSens® Reagent Kits for screening diagnostics**

All AmpliSens® kits for screening detect only high carcinogenic risk genotypes.

AmpliSens® kits detect no less than 11 most widely spread high carcinogenic risk HPV genotypes.

AmpliSens® kits working on the PCR principle in the real-time regime (FRT) allow detection of the exact concentration of the virus (not RLU-conventional fluorescence units) and ration the virus in accordance with the amount of human cells in the analyzed sample, which evens the result variations connected with the inadequate collection of the material. All computations are carried out automatically. The algorithm of detection only of the clinically significant concentration of the virus based on the dilution of the sample has been developed and validated on the clinical material for reagent kits working on the electrophoretic detection or end point fluorescence detection (FEP) principles.

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For diagnostics of high carcinogenic risk papillomavirus infection

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AmpliSens® kits only Russian-made reagent kits for which a large-scale clinical validation was undertaken.

AmpliSens® kits (FRT format) include software that significantly simplifies the results interpretation.

AmpliSens® kits for genetic typing allow differentiation up to 12 most widely spread high risk HPV genotypes: 16, 18, 31, 33, 35, 39, 45, 52, 56, 58, 59, as well as 51 or 66 (depending on the test format).

Recommended instruments for material collection

The material is collected with the help of a cervical cyto-brush with an incision (Yunona model, cat. No.R12-F) into a test tube with the transport medium TCM for the clinical material from the urogenital tract (cat. No. R12-F-100) (pinkish colour).

AmpliSens HPV tests for genetic typing of human papillomavirus

At present there are tests for detection and genetic typing of two most carcinogenic HPV genotypes 16 and 18 as well as tests for genetic typing of a wide range of HPV types (12 genotypes). Tests on 16 and 18 genotypes are available in formats with electrophoretic detection, end point fluorescence detection (FEP) and fluorescence real-time detection (FRT) (three- and more channel units are required). The variant 16, 18 of FRT with real-time detection also allows assessment of the viral load. The tests for genetic typing of a wide range of types are available in formats with electrophoretic detection and real-time detection (a four-channel unit is required).

Characteristics of examined patients and type of clinical material for examination

HPV test is conducted in women. The material for examination is scraping of the cervical canal and/or transformation zone taken by a cytological brush. It's allowed to collect the material for cytological and HPV tests by a single brush: first they take smears-prints and then the brush is placed in the transport medium. On collection of the material the brush is broken and the working part of the brush is kept in the transport medium till delivery to the laboratory. It's allowed to use a universal probe for collection of the material from the cervical canal if the use of the cytological brush is not possible. It's possible to study scrapings from the mucous genital organs and the oral cavity. The study of the vaginal contents or urethra scrapings is less informative than analyses of cervical scrapings, that's why this study is practically not used. The quantitative study for HPV DNA is validated and is used only for the cervical canal material provided all regulations on the material collection, keeping of the brush in the transport medium, use of sorbent methods of DNA isolation are observed (this is especially important for semi-quantitative methods on the basis of the fluorescence end point detection (FEP) and electrophoresis).

Notes on HPV test in men. HPV contamination of men is similar to contamination of women but anatomic peculiarities of the male urogenital tract (no epithelium transformation zone) allow recovery of men without therapy and very often they are cured without treatment and become asymptomatic infection bearers. Owing to the fact that the danger of development of oncological pathology in men is not great and contamination of the female partner doesn’t signify development of the infection clinical manifestations (as the possibility of no-treatment-recovery from the infection (about 80 percent)), HPV screening in men is not recommended. The analysis is carried out only by epidemic indications or for differential diagnostics. It’s necessary to remember that HPV in one of the partners in the absence of HPV in the other or lack of concurrence in the genotypes range of partners is a regular reflection of the virus biology and can’t signify the infidelity of spouses (usually virus elimination occurs within a shorter time for one of the partners, when the couple is infected by several genotypes partners might develop elimination of different types, in this case after recovery from HPV of a certain type secondary contamination doesn’t occur).
HCR HPV SCREEN
Reagent kits for detection of a wide range of high carcinogenic risk HPV genotypes

Advantages of HCR HPV SCREEN kits

- Kits allow detection of the clinical concentration of the virus and its differentiation from the insignificant contamination.
- Kits allow determination of a wide range of high risk genotypes.
- No cross detection of low carcinogenic risk HPV types
- The endogenous internal control principle (human DNA) allows control of stage of DNA isolation and PCR as well as effective evaluation of the quality of the sample collection.
- Convenient, quick and cheap format of PCR in one or two test tubes.

Clinical material for examination

<table>
<thead>
<tr>
<th>Clinical Material</th>
<th>Recommended kits for pre-processing and extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrapses from the cervical canal, transformation zones</td>
<td>DNA-sorb-AM - ( \mathbb{R} ), Mucolysin (for dilution of viscous samples)</td>
</tr>
<tr>
<td>Scrapses from urethra, other mucous tunics</td>
<td>DNA-sorb-AM - ( \mathbb{R} )</td>
</tr>
<tr>
<td>Biopsy samples of mucous tunics and skin</td>
<td>DNA-sorb-C</td>
</tr>
</tbody>
</table>

\( \mathbb{R} \) – a kit is included in the complete set reagent kit

Reagent kits options. FRT format
Fluorescence Detection in Real-Time Regime

<table>
<thead>
<tr>
<th>Cat.No.</th>
<th>Name</th>
<th>Set</th>
<th>No. of tests</th>
<th>Type Mark</th>
<th>Special equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR-V31-T-4x (RG, IQ, Mx)</td>
<td>AmpliSens® HCR HPV screen-titre- FL*</td>
<td>100</td>
<td>Fam, Joe/Hex, Rox, Cy5</td>
<td>Four- and more channel amplifiers: Rotor-Gene 6000 (Corbett Research), iQ5 (BioRad), Mx3000P (Stratagene)</td>
<td></td>
</tr>
<tr>
<td>R-V31-T-4x (RG, IQ, Mx)</td>
<td>AmpliSens® HCR HPV screen-titre- FL*</td>
<td>108</td>
<td>Fam, Joe/Hex, Rox, Cy5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR-V31-T-2x (RG, IQ, SC)</td>
<td>AmpliSens® HCR HPV screen-titre- FL#</td>
<td>100</td>
<td>Fam, Joe/Hex</td>
<td>Two- and more channel amplifiers: Rotor-Gene 6000 (Corbett Research), iQCyCycler (BioRad), SmartCyCycler (Cepheid)</td>
<td></td>
</tr>
<tr>
<td>R-V31-T-2x (RG, IQ, SC)</td>
<td>AmpliSens® HCR HPV screen-titre- FL#</td>
<td>108</td>
<td>Fam, Joe/Hex</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

12 types of HCR HPV types are detected: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59.

* - analysis in one test tube; phylogenetic groups are detected separately
# - analysis in two test tubes

Format advantages

- The first quantitative test for HCR HPV, allows not only exact determination of the clinically important concentration of the virus but detection of the increased virus load and control of the infection course.
- Automatic results interpretation.

Analytical properties

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>1 x 10^3 – 5 x 10^6 GE per ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>No cross reactions for low carcinogenic risk HPV, cutaneous HPV types, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin.</td>
</tr>
</tbody>
</table>

Results of clinical studies

Testing of kits was conducted in 4 thousand patients of the cervical pathology center simultaneously with the cytological, colposcopic and histological examination methods. The diagnostic sensitivity of kits with regard to H-SIL and cervical cancer made 98 percent, the diagnostic specificity (detection only of the clinically significant contamination) in relation to dysplasia of the cervical epithelium - 82 percent.
FEP Format. End Point Fluorescence Detection

<table>
<thead>
<tr>
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<td>AmpliSens® HCR HPV screen-FL#</td>
<td>100</td>
<td></td>
<td>Fam, Hex</td>
<td></td>
<td>Amplifiers Rotor-Gene 6000 (Corbett Research), two-channel amplifiers: Jin (DNA-Technology), AJA-1 (BioSan)</td>
</tr>
<tr>
<td>V31-FEP</td>
<td>AmpliSens® HCR HPV screen-FL#</td>
<td>120</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TV31-3x-FEP</td>
<td>AmpliSens® HCR HPV screen-FL*</td>
<td>100</td>
<td></td>
<td>Fam, Hex, Rox</td>
<td></td>
<td>Amplifiers Rotor-Gene 6000 (Corbett Research), two-channel amplifiers: Jin (DNA-Technology), AJA-1 (BioSan), four-channel amplifier: Jin (DNA-Technology)</td>
</tr>
<tr>
<td>V31-3x-FEP</td>
<td>AmpliSens® HCR HPV screen-FL*</td>
<td>120</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

11 types of HCR HPV types are detected: 16, 18, 31, 33, 35, 39, 45, 52, 56, 58 & 59;
# - analysis in two test tubes, the most carcinogenic genotype 16 is detected separately;
* - analysis in one test tube

Analytical properties

- Sensitivity: \( 1 \times 10^3 \) GE per ml
- Specificity: No cross reactions for low carcinogenic risk HPV, cutaneous HPV types, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin. The supposedly high risk genotype 67 is detected.

Results of clinical studies

Testing of kits was conducted in 700 patients of the cervical pathology center and family planning and reproduction center simultaneously with the cytological, colposcopical and histological examinations. The diagnostic sensitivity of kits with regard to H-SIL and cervical cancer made 97 percent, the diagnostic specificity (detection only of the clinically significant contamination) in relation to dysplasia of the cervical epithelium - 84 percent.

Eph Format - Electrophoretic Detection

Attention! The technology presents danger of contamination! A separate room and personnel are required for the detection!

<table>
<thead>
<tr>
<th>Cat.No.</th>
<th>Name</th>
<th>Set</th>
<th>No. of tests</th>
<th>Type</th>
<th>Special equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV31-100F</td>
<td>AmpliSens® HCR HPV screen-EPh*</td>
<td>100</td>
<td></td>
<td></td>
<td>Electrophoretic chamber, gel-documentation system</td>
</tr>
<tr>
<td>V31-100F</td>
<td>AmpliSens® HCR HPV screen-EPh*</td>
<td>110</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TV31-50F</td>
<td>AmpliSens® HCR HPV screen-EPh#</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14 types of HCR HPV are detected: 16, 18, 31, 33, 35, 39, 45, 52, 53, 56, 58, 59, 66, 70.

Analytical properties

- Sensitivity: \( 5 \times 10^3 \) GE per ml
- Specificity: No cross reactions for low carcinogenic risk HPV, cutaneous HPV types, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin. Detected genotypes 53, 66 and 70 belong to the supposedly high risk group.

Results of clinical studies

Testing of kits was conducted in 1500 patients of the cervical pathology center simultaneously with the cytological, colposcopical and histological examinations. The diagnostic sensitivity of kits with regard to H-SIL and cervical cancer made 98 percent, the diagnostic specificity (detection only of the clinically significant contamination) in relation to dysplasia of the cervical epithelium - 81 percent.

Representative works. FEP format

<table>
<thead>
<tr>
<th>Test Tube 1</th>
<th>Test Tube 2</th>
<th>Test Tube 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV type</td>
<td>signal</td>
<td>HPV type</td>
</tr>
<tr>
<td>31</td>
<td>4-7</td>
<td>18</td>
</tr>
<tr>
<td>35</td>
<td>4-7</td>
<td>33</td>
</tr>
<tr>
<td>39</td>
<td>3,5-6</td>
<td>45</td>
</tr>
<tr>
<td>59</td>
<td>3,5-6</td>
<td>52</td>
</tr>
<tr>
<td>16</td>
<td>(channel HEX)</td>
<td>7-12</td>
</tr>
</tbody>
</table>

Variant “2x”: 2 test tubes, 2 channels

Representative works. Eph format

Clinical samples

Attention! The technology presents danger of contamination! A separate room and personnel are required for the detection!

<table>
<thead>
<tr>
<th>Cat.No.</th>
<th>Name</th>
<th>Set</th>
<th>No. of tests</th>
<th>Type</th>
<th>Special equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV31-100F</td>
<td>AmpliSens® HCR HPV screen-EPh*</td>
<td>100</td>
<td></td>
<td></td>
<td>Electrophoretic chamber, gel-documentation system</td>
</tr>
<tr>
<td>V31-100F</td>
<td>AmpliSens® HCR HPV screen-EPh*</td>
<td>110</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TV31-50F</td>
<td>AmpliSens® HCR HPV screen-EPh#</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14 types of HCR HPV are detected: 16, 18, 31, 33, 35, 39, 45, 52, 53, 56, 58, 59, 66, 70.

Analytical properties

- Sensitivity: \( 5 \times 10^3 \) GE per ml
- Specificity: No cross reactions for low carcinogenic risk HPV, cutaneous HPV types, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin. Detected genotypes 53, 66 and 70 belong to the supposedly high risk group.

Results of clinical studies

Testing of kits was conducted in 1500 patients of the cervical pathology center simultaneously with the cytological, colposcopical and histological examinations. The diagnostic sensitivity of kits with regard to H-SIL and cervical cancer made 98 percent, the diagnostic specificity (detection only of the clinically significant contamination) in relation to dysplasia of the cervical epithelium - 81 percent.

Representative works. EPh format

Clinical samples

Attention! The technology presents danger of contamination! A separate room and personnel are required for the detection!

<table>
<thead>
<tr>
<th>Cat.No.</th>
<th>Name</th>
<th>Set</th>
<th>No. of tests</th>
<th>Type</th>
<th>Special equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV31-100F</td>
<td>AmpliSens® HCR HPV screen-EPh*</td>
<td>100</td>
<td></td>
<td></td>
<td>Electrophoretic chamber, gel-documentation system</td>
</tr>
<tr>
<td>V31-100F</td>
<td>AmpliSens® HCR HPV screen-EPh*</td>
<td>110</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TV31-50F</td>
<td>AmpliSens® HCR HPV screen-EPh#</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14 types of HCR HPV are detected: 16, 18, 31, 33, 35, 39, 45, 52, 53, 56, 58, 59, 66, 70.

Analytical properties

- Sensitivity: \( 5 \times 10^3 \) GE per ml
- Specificity: No cross reactions for low carcinogenic risk HPV, cutaneous HPV types, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin. Detected genotypes 53, 66 and 70 belong to the supposedly high risk group.

Results of clinical studies

Testing of kits was conducted in 1500 patients of the cervical pathology center simultaneously with the cytological, colposcopical and histological examinations. The diagnostic sensitivity of kits with regard to H-SIL and cervical cancer made 98 percent, the diagnostic specificity (detection only of the clinically significant contamination) in relation to dysplasia of the cervical epithelium - 81 percent.
HCR HPV GENOTYPE
Reagent kits for genetic typing of a wide range of high carcinogenic risk HPV genotypes

Advantages of HCR HPV GENOTYPE kits

- Kits allow detection and determination of a wide range of HCR HPV to a precision of a type (12 types).
- No cross detection of low carcinogenic risk HPV types
- The endogenous internal control principle (human DNA) allows control of stage of DNA isolation and PCR as well as effective evaluation of the quality of the sample collection.
- Convenient format of multiprime PCR—12 types in four test tubes.

Clinical material for examination

<table>
<thead>
<tr>
<th>Clinical Material</th>
<th>Recommended kits for pre-processing and extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrapes from the cervical canal, transformation zones</td>
<td>DNA-sorb-AM</td>
</tr>
<tr>
<td>Scrapes from urethra, other mucous tunics</td>
<td>DNA-sorb-AM</td>
</tr>
</tbody>
</table>

Reagent kits options. FRT format Real-time fluorescence detection

<table>
<thead>
<tr>
<th>Cat.No.</th>
<th>Name</th>
<th>Set</th>
<th>No. of tests</th>
<th>Type</th>
<th>Mark</th>
<th>Special equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR-V25(RG, iQ, Mx)</td>
<td>AmpliSens® HCR HPV FL-genotype</td>
<td>100</td>
<td>Fam, Joe, Hex, Rox, Cy5</td>
<td>Four- and more channel amplifiers: Rotor-Gene 6000 (Corbett Research), IQ5 (BioRad), Mx3000P (Stratagene)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R-V25(RG, iQ, Mx)</td>
<td>AmpliSens® HCR HPV FL-genotype</td>
<td>108</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FRT format advantages

- The first real-time test for genotype determination.
- No time-consuming hybridization stage, genetic typing is carried out simultaneously with amplification.
- Automatic results registration, no subjectivity of evaluation.

Interpretation of results

<table>
<thead>
<tr>
<th>Lid colour</th>
<th>Fam</th>
<th>Joe</th>
<th>Rox</th>
<th>Cy5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>16</td>
<td>31</td>
<td>18</td>
<td>BK</td>
</tr>
<tr>
<td>Red</td>
<td>39</td>
<td>45</td>
<td>59</td>
<td>BK</td>
</tr>
<tr>
<td>Green</td>
<td>33</td>
<td>35</td>
<td>56</td>
<td>BK</td>
</tr>
<tr>
<td>Orange</td>
<td>58</td>
<td>52</td>
<td>51</td>
<td>BK</td>
</tr>
</tbody>
</table>

Analytical properties

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>1 x10^3 GE per ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>100% type specificity, no cross reactions for any HPV different from the analyzed genotype, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin.</td>
</tr>
</tbody>
</table>
Results of clinical studies

Testing of kits was carried out on 251 HPV-positive sample in comparison with universal primers MY11/09, GP5+/6+ with subsequent genetic typing by a hybridization or sequencing method. Complete concurrence of genetic typing results was observed in 92.4 percent of cases and the remaining 4.8 percent of unmatched results is related to detection by the kit AmpliSens HCR HPV-genotype-FL of a greater amount of genotypes than the comparison systems revealed – the diagnostic accuracy is 97.2 percent. Comparison of analytical properties of kits with the common method of detection and genetic typing of HPV based on primers MY11/09 and GP5+/6+ showed that a reagent kit AmpliSens possesses a constant level of sensitivity whereas the sensitivity of a MY/GP+-based system depends on the genotype.

Representative works. EPh format

Test tube 1 "16-35"

Test tube 2 "18-59"

Test tube 3 "52-66"

Explanation:

Configuration of kits:

- a "complete set reagent kit" includes reagents for extraction, amplification and detection;

- an "amplification reagent kit" (PCR-set) includes only amplification reagents.

Kit types:

"Hot Start" is provided by a modified polymerase (TaqF) activated at heating:

- a set includes vials with reagents not dispensed into PCR test tubes, a modified polymerase TaqF is used.

Eph Format - Electrophoretic Detection

Attention! The technology presents danger of contamination! A separate room and personnel are required for the detection!

Analytical properties

Results of clinical studies

Testing of kits was carried out on 213 HPV-positive samples in comparison with universal primers MY11/09, GP5+/6+ with subsequent genetic typing by a hybridization or sequencing method. Complete concurrence of genetic typing results was observed in 87.8 percent of cases and the remaining 8.5 percent of the unmatched detected genotypes is related to differences in analytical sensitivity of methods for various genotypes, and only in 3.7 percent of cases different results of typing were observed – diagnostic precision making 96.3 percent.

Interpretation of results

<table>
<thead>
<tr>
<th>HPV type</th>
<th>Fragment size, p.n.</th>
<th>HPV type</th>
<th>Fragment size, p.n.</th>
<th>HPV type</th>
<th>Fragment size, p.n.</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>325</td>
<td>18</td>
<td>425</td>
<td>52</td>
<td>360</td>
</tr>
<tr>
<td>31</td>
<td>520</td>
<td>39</td>
<td>340</td>
<td>56</td>
<td>325</td>
</tr>
<tr>
<td>33</td>
<td>227</td>
<td>45</td>
<td>475</td>
<td>58</td>
<td>240</td>
</tr>
<tr>
<td>35</td>
<td>280</td>
<td>59</td>
<td>455</td>
<td>66</td>
<td>304</td>
</tr>
</tbody>
</table>

M 16 31 33 35 M 18 39 45 59 M 52 56 58 66

Internal control

HPV genotypes

Sensitivity for certain genotypes (on ten-fold dilutions of control samples)}
16 and 18 HPV types
Reagent kits for detection and separate determination of 16 and 18 HPV genotypes

Advantages of 16 and 18 genotypes HPV
- Kits allow detection of the two most carcinogenic HPV types.
- Kits allow differentiation of 16 and 18 genotypes.
- No cross detection of other HPV genotypes.
- The endogenous internal control principle (human DNA) allows control of stage of DNA isolation and PCR as well as effective evaluation of the quality of the sample collection.
- Convenient and quick format of PCR in a single test tube.

Clinical material for examination
- Recommended kits for pre-processing and extraction
  - Scrapes from the cervical canal, transformation zones: DNA-sorb-AM
  - Scrapes from urethra, other mucous tunics: DNA-sorb-AM
  - Biopsy samples of mucous tunics and skin: DNA-sorb-C

Reagent kits options. FRT format
Fluorescence Detection in Real Time

Calibrating line

FRT format advantages
- Quantitative test for HPV of 16 and 18 types allows not only determination of 16 and 18 virus genotypes but determination of the viral load.
- Automatic results interpretation.

Analytical properties
- Sensitivity: 1 x 103 GE per ml
- Specificity: No cross reactions for high carcinogenic types different from 16 and 18, low carcinogenic risk HPV, cutaneous types of HPV, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin.

Results of clinical studies
Testing of kits was carried out on 580 HPV-positive samples in comparison with a complete set of HCR HPV GENOTYPE. Complete concurrence of results of detection and determination of 16 and 18 genotypes was observed in 98.9 percent of cases, one sample produced a discordant result but the data on content of HCR HPV in it (less than 10 HPV copies per reaction) point out the possibility of non-reproducibility of the testing result due to a small amount of DNA-target.
FEP Format.  
**End Point Fluorescence Detection**

<table>
<thead>
<tr>
<th>Cat.No.</th>
<th>Name</th>
<th>Set</th>
<th>No. of tests</th>
<th>Type</th>
<th>Mark</th>
<th>Special equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>V12-FEP</td>
<td>AmpliSens® HCR 16/18-FL</td>
<td></td>
<td>120</td>
<td>Fam, Hex, Rox</td>
<td></td>
<td>Amplifiers Rotor-Gene 6000 (Corbett Research), three- and more channel amplifiers: ALA-1 (BioSan), four-channel amplifier Jin (DNA-Technology)</td>
</tr>
</tbody>
</table>

Analytical properties

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>1 x10^3 GE per ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>No cross reactions for high carcinogenic types different from 16 and 18, low carcinogenic risk HPV, cutaneous types of HPV, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin.</td>
</tr>
</tbody>
</table>

Results of clinical studies

Testing of the kit were conducted simultaneously with the kit AmpliSens® HPV 16/18 FL on 289 HPV-positive samples and in comparison with the kit AmpliSens® HCR HPV-genotype. Complete matching of detection and determination of 16 and 18 genotypes is established in 100 percent of cases.

Eph Format - Electrophoretic Detection

**Attention! The technology presents danger of contamination!**  
*A separate room and personnel are required for the detection!*

<table>
<thead>
<tr>
<th>Cat.No.</th>
<th>Name</th>
<th>Set</th>
<th>No. of tests</th>
<th>Type</th>
<th>Special equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>V12-100-R0,5</td>
<td>AmpliSens® HPV 16/18-EPh</td>
<td></td>
<td>110</td>
<td></td>
<td>Electrophoretic chamber, gel-documentation system</td>
</tr>
<tr>
<td>V12-100-R0,2</td>
<td>AmpliSens® HPV 16/18-EPh</td>
<td></td>
<td>110</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V12-200</td>
<td>AmpliSens® HPV 16/18-EPh</td>
<td></td>
<td>220</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Analytical properties

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>2 x10^3 GE per ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>No cross reactions for high carcinogenic types different from 16 and 18, low carcinogenic risk HPV, cutaneous types of HPV, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin.</td>
</tr>
</tbody>
</table>

Results of clinical studies

Testing of kits were carried out on 118 HPV-positive samples in comparison with universal primers MY11/09, GP5+/6+ with subsequent genetic typing by a hybridization or sequencing method. In case of a discordant result they undertook sequencing of the DNA fragment amplified in a kit. Complete concurrence of genetic typing results on detection of 16 an 18 HPV types as compared to MY/GP and hybridization was observed in 90.6 percent of cases, in all the remaining cases sequencing of the amplified segment confirmed presence of HPV of 16 or 18 types and the obtained discordances are most likely related to a lower analytical sensitivity of MY and GP primers. Thus, the precision of determination of 16 and 18 types made 100 percent.

Representative works. FEP format

<table>
<thead>
<tr>
<th>Channel 1</th>
<th>Channel 2</th>
<th>Channel 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV type</td>
<td>signal</td>
<td>IC</td>
</tr>
<tr>
<td>16</td>
<td>7-10</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Representative works. EPh format

Explaination:

**Configuration of kits:**
- a "complete set reagent kit" includes reagents for extraction, amplification and detection;
- an "amplification reagent kit" (PCR-set) includes only amplification reagents.

Kit types:
"Hot Start" is provided by a wax layer:
- a set includes ready to use PCR test tubes with the lower mixture applied under the wax
- a set includes vials with reagents not dispensed into PCR-test tubes.

"Hot Start" is provided by a modified polymerase (TaqF) activated at heating:
- a set includes vials with reagents not dispensed into PCR test tubes, a modified polymerase TaqF is used.
Low Carcinogenic Risk Human Papillomaviruses (LCR HPV)

Major low-carcinogenic risk HPV genotypes: 6, 11, 42, 43, 44

A group of low carcinogenic risk HPV is represented by more than 10 genotypes among which the genotypes 6 and 11 are of greatest importance as they are responsible for the overwhelming amount of low-carcinogenic pointed condylomas of genital organs and for more than 90 percent of cases of condylomatosis of the larynx in children. The characteristic property of the infection is a large share of spontaneous recoveries within one year from the contamination moment without development of clinical manifestations of the infection (pointed condylomas). With that latent and sub-clinical infection forms do not present any danger. This fact defines peculiarities of diagnostics.

Indications for the examination:

- Differential diagnostics with high carcinogenic types
- Differential diagnostics with diseases of non papillomavirus etiology
- Examination of pregnant women and newborns
- In addition to this, indications to examination for low-carcinogenic HPV types include:
  - Differential diagnostics with high-carcinogenic risk HPV;
  - Differential diagnostics with other infections (e.g. atypical course of the herpes-virus infection).

Detection of HPV 6 and 11 genotypes is sufficient for diagnostics as they are associated with more than 90 percent of clinical forms of low carcinogenic papillomavirus infection. Detection of 5 HPV genotypes: 6, 11, 42, 43, 44 - might be considered optimum.

Counter-indications to examination

Prophylactic medical examination in absence of clinical manifestations

Diagnostics of the papillomavirus infection of low risk

The major informative diagnostic marker of the papillomavirus infection of low risk is detection of pointed condylomas (clinical form) by a doctor at examination.

Cytological examination

Cytological examination is not used for diagnostics of low-carcinogenic risk infections due to the fact that objectives of the cytological examination are detection of precancer changes of the epithelium. But contamination with low risk HPV is accompanied by development of light dysplasias detected only by cytological examination as L-SIL, which leads to reduction of the cytology specificity (repeated examinations and/or colposcopy are required).

Molecular-biological examination methods

Molecular-biological examination methods (including PCR) might be used to diagnose papillomavirus infection of a low carcinogenic risk. But it’s necessary to remember that this method allows determination of not only clinical but sub-clinical and latent forms of the infection. Detection of the latter is low informative since:

- Low-carcinogenic risk HPV have low carcinogenic potential (relatively safe);
- Early infection detection (before appearance of clinical manifestations) is not justified as the majority of the infected people recover without treatment. In addition to this, the effective etiotropic therapy on the latent infection stage is not yet developed.

This implies that detection of the fact of the low carcinogenic risk HPV at scheduled examinations and prophylactic medical examinations is not justified in the majority of cases. Examination of pregnant women makes an exception. Detection of low-carcinogenic risk HPV at pregnancy or at the stage of its planning is the reason of awareness in relation to a possibility of development of larynx papillomatosis in the baby. But treatment of latent and sub-clinical infection of the pregnant woman or Caesarian delivery are not correct therapeutic tactics as they have no proper effectiveness and practicability. Meticulous care of the baby is the only justified measure.

6 and 11 HPV genotypes
Reagent kits for detection and separate determination of 6 and 11 HPV genotypes

Advantages of 6 and 11 HPV kits

- Kits allow detection of the two most widely spread low carcinogenic risk HPV
- Kits allow differentiation of 6 and 11 genotypes.

Clinical material for examination

<table>
<thead>
<tr>
<th>Clinical Material</th>
<th>Recommended kits for pre-processing and extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrapes from mucous tunics (oral cavity, urethra, cervical canal, mucous tunics of other locations), scrapings of condylomas</td>
<td>DNA-sorb-AM®, Mucolyzin (for dilution of viscous samples)</td>
</tr>
<tr>
<td>Biopsy samples of mucous tunics and skin</td>
<td>DNA-sorb-C</td>
</tr>
</tbody>
</table>

- a kit is included in the complete set reagent kit (®)
Results of clinical studies

Testing of kits was carried out on 385 HPV-positive samples in comparison with universal primers MY11/09, GP5+/6+ with subsequent genetic typing by hybridization or a sequencing method. In case of a discordant result they undertook sequencing of the DNA fragment amplified in a kit. Complete concurrence of genetic typing results on detection of 6 and 11 HPV types as compared to MY/GP and hybridization was observed in 88.2 percent of cases, sequencing of the amplified segment confirmed presence of HPV of 6 or 11 types in 97.1 percent of cases, one sample (2 percent) contained insufficient amount of DNA and remained unconfirmed. Thus, the precision of determination of 6 and 11 types made 97.1 percent.

Sensitivity

$2 \times 103$ GE per ml

Specificity

No cross reactions for low carcinogenic types different from 6 and 11, high carcinogenic risk HPV, cutaneous types of HPV, for human DNA as well as for microorganisms present in the urogenital canal, oral cavity, skin.

FRT format advantages

- Detection and determination of 6 and 11 HPV in a single test tube.
- Automatic results interpretation

On sale soon:

- reagent kits for determination of a wide range of low-carcinogenic types of HPV in FEP and FRT formats

Explanation:

**Configuration of kits:**

- a “complete set reagent kit” includes reagents for extraction, amplification and detection;
- an “amplification reagent kit” (PCR-set) includes only amplification reagents.

**Kit types:**

“Hot Start” is provided by a wax layer:

- a set includes ready to use PCR test tubes with the lower mixture applied under the wax
- a set includes vials with reagents not dispensed into PCR test tubes

“Hot Start” is provided by a modified polymerase (TaqF) activated at heating:

- a set includes vials with reagents not dispensed into PCR test tubes, a modified polymerase TaqF is used