Human Papillomavirus DNA Diagnostic Kit (PCR-Fluorescence Probing)

Product Identification

Product Name: Human Papillomavirus DNA Diagnostic Kit (PCR-Fluorescence Probing)
Reference Number: S3057E
Package Specification: 48 tests/kit, Pre-packaged 24 tests/kit, Pre-packaged 12 tests/kit

Intended Use

The Human Papillomavirus DNA Diagnostic Kit (PCR-Fluorescence Probing) is intended for the qualitative detection of 15 kinds of high-risk human papillomavirus (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68) DNA in exfoliated cells from females' cervix, and also for the subtype identification of HPV16 and HPV18.

For in vitro diagnostic use only. For professional use only.

Test principle summary and explanation

Summary

Clinical background: Human papillomavirus (HPV) is a non-enveloped double-stranded circular DNA virus of small molecular weight. It infects and parasitizes epithelial cells of human reproductive organs and other organs. HPV falls into two types clinically, high-risk and low-risk HPV, according to the different degrees of pathogenicity or carcinogenic risk of different subtypes. Low-risk HPV mainly causes pathological changes such as exogeneity wart in anal skin, male external genitalia, female labia, urethral orifice and vagina lower segment, and low-grade cervical intraepithelial neoplasia. High-risk HPV can cause not only external genital warts, but more seriously, external genital cancer, cervical carcinoma and high-grade cervical intraepithelial neoplasia. The study shows that the persistent infection of HPV is the main cause of cervical carcinoma and precancerous lesion[1].Studies show the persistent infection of human papillomavirus is the main cause of cervical carcinoma and precancerous lesion. High-risk HPV DNA can be detected in 99.7% patients with cervical carcinoma. Because of the close relationship between high-risk HPV and cervical carcinoma, it is a significant screening method to test HPV for cervical carcinoma[2.3].

Base on the study results by WHO International Agency for Research on Cancer (IARC) and other international organizations, the 13 kinds of genotypes including HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68 are classified as high-risk HPV, and the 5 kinds of genotypes including HPV26, 53, 66, 73, 82 are classified as medium-risk HPV. This diagnostic kit chooses the above 13 kinds of high-risk genotypes and two popular kinds of medium-risk genotypes that are HPV53 and 66 to be the target genotypes, in order to guarantee that the kit is capable of cervical carcinoma screening and risk evaluation. Moreover, it is clearly indicated that the females at the age of 30 or above who have no abnormal cervical cytology but the HPV detection is positive, especially for HPV16 and HPV18 infected females, should get vaginoscopy immediately[4,5]. Therefore, the kit can be used for detection of the 15 kinds of target genotypes and also subtype identification of HPV16 and HPV18.

So far, it is difficult to test HPV by the use of conventional virus culture or serological technology. The main detection technology used in laboratory is molecular biological methods based on nucleic acid test. There are two main methods in this technology, one method based on target sequence amplification: type-specific PCR, mRNA amplification test, primer PCR, real-time (multiplex) PCR fluorescence technology, etc.[6.7], and the other method based on signal amplification technique: Amplification technique of liquid phase, morphology, enzyme digestion, etc.

Test principle

By applying real-time fluorescence quantitative PCR technology, this diagnostic kit uses several pairs of specific primers and fluorescence probes which are designed to target nucleic acid conserved sequences of the above mentioned 15 kinds of genotypes, accompanied with other ingredients in High-risk HPV-PCR mix, to achieve detection of the 15 types of virus samples and subtype identification of HPV16 and HPV18, through the changes of the four fluorescent signals (FAM, HEX/VIC, ROX, CY5).

The PCR detection system uses UNG enzyme + dUTP contamination-proof system to fully degrade possible PCR amplified products in order to avoid a false positive result.

The PCR detection system uses a positive control to monitor β-globin in human epidermal cells for the evaluation of amplification reaction of samples and monitor the presence of PCR inhibitors, as well as to evaluate the nucleic acid extraction efficiency, in order to avoid a false negative result.

The FAM channel of this diagnostic kit is used to test HPV 18-DNA, HEX channel to test β-globin, ROX channel to test HPV 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68-DNA, and CY5 to test HPV 16-DNA.

Materials provided

This kit is an amplification reaction reagent and contains the following components:

No.	Reagent Name	Specification & Qty.			Main Ingredients
		48T	Pre-packaged 24T	Pre-packaged 12T	
1	HPV-Enzyme Mix	192 μL/tube × 1 tube	4 μL/tube × 24 tubes	4 μL/tube × 12 tubes	DNA polymerase, Uracil-N-Glycosylase enzyme
2	HPV-PCR Mix	864 μL/tube × 2 tubes	36 μL/tube × 24 tubes	36 μL/tube × 12 tubes	Primers, Probes, dNTPs, $MgCl_2$, PCR buffer
3	HPV-Negative Control	1000 μL/tube × 1 tube	1000 μL/tube × 1 tube	1500 μL/tube × 1 tube	Normal saline
4	HPV-Positive Control	50 μL/tube × 1 tube	50 μL/tube × 1 tube	1500 μL/tube × 1 tube	Plasmid containing target gene fragment of HPV16, 18, 45 and β-globin

Materials required but not provided

1. Materials required but not provided: 1.5 mL DNase-free and RNase-free centrifuge tubes, 0.2 mL PCR reaction tubes, pipette tips (10 μL, 200 μL and 1000 μL tips with filters are preferred), desktop centrifuge, desktop vortex mixer, magnetic-bead separator, various models of pipettes.
2. Reagent required but not provided: Cell preservation solution, Nucleic Acid Extraction-Purification Kit (Reference Number: S50016E Series) or Sample Release Reagent (Reference Number: S1013E Series) manufactured by Sansure Biotech Inc.

Warnings and precautions

Warnings

1. Do not mix or exchange components from different kits.
2. All biological materials in the kit have been inactivated.

Precautions

1. For *in vitro* diagnostic use only. Please read the product manual carefully before operation.
2. Please learn and be familiar with the operation procedures and precautions for each instrument before test. Please perform quality control test for each batch of tests.
3. Laboratory management shall strictly follow management practices of PCR gene amplification laboratory; laboratory personnel must receive professional training; test processes must be performed in separated rooms; all consumables should be for single use only after sterilization; special instruments and devices should be used for every process; all lab devices used in different processes and rooms should not be cross-used.
4. All samples for detection should be handled as potentially infectious. Wear laboratory coats, protective disposable gloves and change the gloves often to avoid cross-contamination between samples. Handling of samples and waste must meet relevant requirements outlined in local, state and national regulations.
5. Before use, all reagents must be fully thawed at room temperature and mixed thoroughly.
6. The product performance has been verified only on cervical epithelial cell samples and the samples collection and treatment methods (including sample collection liquids etc.) of section Sample Requirements. Other sample types or sample collection, treatment methods can not guarantee the product performance.
7. After the addition of the sample in the tube the resulting solution is to be considered potentially biohazardous, handle the reagent with appropriate precautions and good laboratory practice.
8. The safe disposal of the reagents supplied must be carried out according to the instruction contained in the specific Safety Data Sheets and in compliance with the national regulations on disposal of potentially hazardous waste.
9. Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established; If you have any questions about the test or the results, please contact Sansure`s customer service hotline +86-731-88883176-6116 or send an email to info@sansure.com.cn/ support@sansure.com.cn.

IVD storage, operating conditions and stability

The shelf life of the kit is 12 months at -25°C to -15°C and protected from light. Please see the manufacturing date and expiry date on the outer package.

1. The reagents keep stable at -25°C to -15°C after opening. Once the reagents are used, the freeze/thaw cycles of the amplification reagent should not exceed five.
2. The reagents keep valid for 5 days during the shipment in a sealed foam box containing ice pack with the temperature lower than 20°C.

Instrumentation

The kit is compatible to Fluorescence Quantitative Analysis System containing FAM, HEX/VIC, CY5 and ROX channels such as:

1. Angilent/AriaDx Real-Time PCR System
2. Applied Biosystems/7500 Real-Time PCR System
3. Bioer/QuantGene 9600 Fluorescent Quantitative Detection System (Model: S-Q96C)
4. Bio-Rad/CFX 96 Deep Well Dx ORM
5. Hongshi/SLAN®-96P Real-Time PCR System
6. Molarray/Real-Time Quantitative Thermal Cycler (Model: MA-6000)
7.Roche/LightCycler® 480 instrument II
8.Sansure/Portable Molecular Diagnostic System (S-Q37A/S-Q37B)
9. Sansure/Portable Molecule Workstation (Model: S-Q36A)
10.Sansure/Portable Molecule Workstation (Model: S-Q31A/S-Q31B)
11.Thermofisher/QuantStudio™ 5 Real-Time PCR System

Collecting and preparing specimens

1. Applicable sample type: exfoliated cells from females' cervix.
2. Collection of specimen

2.1 Requirements before collection:

2.1.1 Sample should not be collected during females' menstrual period.

2.1.2 The subjects should not have sex during the 48 hours before the collection.

2.1.3 The subjects should not have vaginal douching or have vaginal medication like contraceptive salve within 3 days before the collection.

2.2 Steps of using disposable sterile cervical sampler (containing cervical brush and cell preservation solution) to collect the samples are as follows.

For females who have suspected cervical infection, collect exfoliated cells from their cervix.

2.2.1 Use a cotton swab to wipe the excessive secretions on the cervical opening.

2.2.2 Put the cervical brush on the cervical opening and slightly rotate the brush clockwise for three to four circles.

2.2.3 Take out the cervical brush slowly and place it in a sample collection tube containing cell preservation solution.

2.2.4 Break off the brush handle out of the tube, seal it and send for detection.

It is recommended to use Sample Storage Reagent (Reference Number: X1001 Series) manufactured by Sansure Biotech Inc. or PreservCyt® Solution manufactured by Hologic Inc. to preserve samples.

3. Storage and delivery of specimens

Samples collected via the above-mentioned method can be used for immediate detection, or stored at room temperature for up to 24 hours, or at 2-8°C for less than 120 hours, or at -25°C to -15°C for up to 7 months. Freeze/thaw cycles should not exceed seven. Samples should be transported in a sealed frozen pitcher with ice or in a sealed foam box with ice. Keep the sample at -70°C or lower for long term storage. Sample Storage Reagent, such as Sample Storage Reagent (Reference Number:X1006E Series).

Test procedure

1. Please process according to the following steps for 7500 Real-Time PCR System, SLAN®-96P Real-Time PCR System, Real-Time Quantitative Thermal Cycler (Model: MA-6000), QuantGene 9600 Fluorescent Quantitative Detection System (Model: S-Q96C), AriaDx Real-Time PCR System, CFX 96 Deep Well Dx ORM, LightCycler® 480 instrument II and QuantStudio™ 5 Real-Time PCR System instrument:

1.1. Preparation of reagent (performed at "reagent preparation room")

1.1.1 Take all of the components out of the kit and equilibrate them to room temperature, then mix each of them respectively for later use.

1.1.2 According to quantity of samples to be tested,, HPV-Negative Control and HPV-Positive Control, pipette appropriate quantity of HPV-PCR Mix and HPV-Enzyme Mix (HPV-PCR Mix 36 μL/test + HPV-Enzyme Mix 4 μL/test). Fully mix them to make a PCR-Mastermix and centrifuge them at 2000 rpm for 10 seconds. Keep it at 2-8°C for later use.

	1 sample	10 samples	24 samples	48 samples
HPV-PCR Mix (μL)	36	360	864	1728
HPV-Enzyme Mix (μL)	4	40	96	192

Note: The above configuration is just for your reference and to ensure enough volume of the PCR-Mastermix, more volume of the actual pipetting may be required.

1.2. Pretreatment of samples (performed at "sample processing room") (HPV-negative control should be processed and extracted together with samples.)

Pipette 1 mL of sample from the sample collection tube into a 1.5 mL centrifuge tube as the test sample. Refer to the following steps to process the samples.

Method 1: It is recommended to use Sample Release Reagent (Reference Number: S1013E Series) manufactured by Sansure Biotech Inc to extract the nucleic acid as per its instructions.

Method 2: It is recommended to use Multi-type Sample DNA/RNA Extraction-Purification Kit (Magnetic beads method) (Reference Number: S50016E Series) manufactured by Sansure Biotech Inc to extract the nucleic acid as per their instructions.

1.3. Loading of Samples (performed at "sample processing room")

1.3.1 Processing of test samples and HPV-Negative Control: respectively add 10 μL of the pretreated samples and HPV-Negative Control into a PCR reaction tube (avoiding pipetting particulate matters like cell debris, etc.)

Processing of HPV-Positive Control: respectively add 10 μL of HPV-Positive Control into a PCR reaction tube containing.

1.3.2 Add 40 μL of PCR-Mastermixes into each PCR reaction tube. Cover the tube lid (If there are bubbles, flick the tube to remove the bubbles), and centrifuge the tube at 2000 rpm for 10 seconds or lightly swing the tube until there no obvious liquid beads on the wall.

1.4. PCR Amplification (performed at "amplification and analysis room") (Refer to user manual of each instrument for the settings)

1.4.1 Place the PCR reaction tubes into the sample wells of the amplification instrument. Input the settings of HPV-Negative Control, HPV-Positive Control and unknown samples in the corresponding sequence, and input the sample name.

1.4.2 Selection of PCR test channel:

a) Select FAM channel to test HPV18-DNA.

b) Select HEX or VIC channel to test β-globin (Internal Control).

c) Select CY5 channel to test HPV16-DNA.

d) Select ROX channel to test HPV31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68-DNA.

1.4.3 Cycle parameters settings:

	Steps	Temperature	Time	Cycle No.
1	UNG enzyme reaction	50°C	2 min.	1
2	Predenaturation	94°C	5 min.	1
3	Denaturation	94°C	15 sec.	45
	Annealing, extension and fluorescence detection	57°C	30 sec.*	
4	Device cooling (optional)	25°C	10 sec.	1

***Note:** Due to the device ABI 7500's technical specifications, it cannot be set at 30 sec., but can be set at 31 sec. or 32 sec. When the settings are completed, save the settings and carry out the reaction procedure.

2. Please process according to the following steps for Portable Molecule Workstation (Model: S-Q31A/S-Q31B):

2.1 Preparation of consumables and reagents

(1)Take out the reaction tube carrier, PCR reaction tube and Tip.

(2)Put the tip into **Well H**, the PCR reaction tube into **Well PCR** (The well location information has been marked on the reaction tube carrier).

(3)Put Sample Release Reagent (Reference Number: S1013E Series) into the **Well B**; put HPV-PCR Mix into the **Well C**; Put HPV-Enzyme Mix into the **Well D**.

(4)Add 20μL sample to be tested or HPV-Positive Control or HPV-Negative Control into the **Well B**. (To avoid bubbles during operation, it is recommended to pipet deeply and release slowly).

2.2 Test Procedure (Refer to user manual of each instrument to adjust the settings.)

2.2.1 Gently press the front door to open it.

2.2.2 Place the **Well A** of reagent strip into the instrument towards the outside of the instrument.

2.2.3 Click the "**Lab task**" on the instrument display screen to enter the interface of setting new lab task.

2.2.4 Select the required lab project in the drop-down menu of **Lab project**, enter the corresponding task name in the **Task Name** bar, and input and select other items that should be input or selected.

2.2.5 Click **"Submit"** to submit the lab task and **"OK"** to run the instrument and start the lab task successively.

2.2.6 When the Portable Molecule Workstation (Model: S-Q31B) shows **"Please transfer the PCR tube to the 1/2/3/4"** (The S-Q31A shows "Please transfer the PCR tube") on the interface, take out the PCR tube and cover it well, then centrifuge it instantaneously.

2.2.6 Insert the PCR tube into the PCR amplification module (the "PCR 1/2/3/4" cover has been automatically opened at this time), close the PCR lid of the amplification module, then click **"OK"** for amplification detection.

3. Please process according to the following steps for Portable Molecular Workstation (Model: S-Q36A):

3.1 Preparation of consumables and reagents

(1) Take out the Consumables kits and reagents.

(2) Put Sample Release Reagent (Reference Number: S1013E Series) into the **Well B**; Put HPV-PCR Mix into the **Well C**; Put HPV- Enzyme Mix into the **Well D**, (The well location information has been marked on the carrier set).

(3) Add 20μL sample to be tested or HPV-Positive Control or HPV-Negative Control into the **Well B** (To avoid bubbles during operation, it is recommended to pipet deeply and release slowly).

3.2 Test Procedure (Refer to user manual of each instrument to adjust the settings.)

3.2.1 Click the "and" button on the instrument display screen to open the door of the instrument and put the prepared consumables into the designated position of the instrument.

3.2.2 Click the **"New"** on the instrument display screen to enter the new experiment task setting interface.

3.2.3 Select the required lab project in the drop-down menu of **Lab project**, enter the corresponding task name in the **Task Name** bar, and input and select other items that should be input or selected.

3.2.4 Click **"Submit"** to submit the lab task and **"OK"** to run the instrument and start the lab task successively.

4. Please process according to the following steps for Portable Molecular Diagnostic System (S-Q37A/S-Q37B):

4.1 Pre-run preparation

4.1.1 Load the amplification reagent component assembly into the extraction reagent component (Nucleic Acid Extraction-Purification Kit, Reference Number : S50016E-12A) to compose the test reagent cartridge;

4.1.2 Open the seal plug of the sample loading hole, add 350μL sample or HPV-Positive Control or HPV-Negative Control into the sample loading hole (To ensure Diagnostic System have 300μL samples for nucleic acid extraction); or use transfer pipet from the extraction reagent kit to pipette sample into the sample loading hole (When sample enter the lower bubble of transfer pipet indicates enough sample has been taken). Then close the seal plug.

4.2 Test Procedure

4.2.1 Click the "**Specimen**" button on the instrument display screen to open the door of the instrument and enter the new experiment task setting interface.

4.2.2 Put the prepared consumables into the designated position of the instrument.

4.2.3 Enter specimen information, select the required experimental project in the drop-down menu of Experimental project, enter the corresponding task name in the **Task Name** bar, and input and select other items that should be input or selected.

4.2.4 Click "**Submit**" to submit the lab task and "**OK**" to run the instrument.

Reading test results

1. Result analysis (Refer to user manual of each instrument for the settings)

Results will be saved automatically when reactions are completed. Adjust Start, End and Threshold values of Baseline of the graph according to analysis results (Users can adjust the values according to the actual situation. Start value can be set between 3-15, and End value between 5-20. Adjust the amplification curve of negative control to be flat or below threshold). Click "**Analyze**" to implement the analysis and make sure each parameter satisfies the requirements given in "5. Quality Control". Go to "**Plate**" window to record Ct value.

2. Quality control

The test result is treated as valid if all the conditions in the table below are met for the same test. Otherwise, the test result is treated as invalid and needs to be repeated.

	HPV-Positive Control	HPV-Negative Control
Ct Value	24-30 at FAM, HEX/VIC, CY5 and ROX channel; amplification curve of sample is like "S" shape.	No display at FAM, HEX/VIC, CY5 and ROX channel.

Positive Reference Values

Through the research on reference value (ROC curve method), the Ct positive reference value of the kit for detecting the target gene is determined to be 39, and the Ct positive reference value for detecting the internal control is to be 40.

Interpretation of test results

1. Determination of negative or positive results

Conclusion	Ct value of sample at FAM, CY5 and ROX channel	Ct value of internal control at HEX/VIC channel
Positive	≤ 39	≤ 40
Others*	≤ 39	> 40 or N/A
Negative**	>39 or N/A	≤ 40
Invalid***	>39 or N/A	> 40 or N/A

Note: * This suggests that there are no cervical epithelial cells in the sample, but the patient has recently been exposed to HPV, so it can not be determined whether the patient is infected with HPV. It is suggested to collect the sample again for detection.

** It includes that the concentration of high-risk HPV DNA is lower than the limit of detection or below the predetermined positive value.

*** This suggests an investigation should be carried out to find out the reasons when Ct value of the internal control is > 40 or N/A and repeat it. (If repeated tests still produce invalid results, please contact Sansure Biotech at info@sansure.com.cn)

2. Subtype identification results

Determine the subtype identification result of high-risk human papillomavirus (15 types) according to the table below:

Detection result	Subtype identification
Sample is detected positive at CY5 channel.	HPV16 positive
Sample is detected positive at FAM channel.	HPV18 positive
Sample is detected positive at ROX channel.	Other high-risk HPV positive

Limitations of the procedure

1. This diagnostic kit can be only used for the detection of the 15 types of high-risk human papillomavirus, which are HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68.
2. The detection results can be combined with cervix cytologic test results and other related medical examination results to comprehensively analyze the disease, but can not be used alone as the basis of patient management.
3. Possible reasons for a false negative result:
3.1 Incorrect collection, delivery and processing, low viral titration may all result in a false negative result.
3.2 Mutations in high-risk HPV target sequence or sequence change due to other causes may result in a false negative result.
3.3 Incorrect storage of diagnostic kits may result in a false negative result.
3.4 Other unproved interference or PCR inhibitors may also result in a false negative result.
4. Cross-contamination occurring in sample processing may result in a false positive result.

Performance characteristics

1. Accuracy

When the kit is used to detect national genotype references of different genotypes or the standardized enterprise's work references, the results are all positive, and the subtype identifications of HPV16 and HPV18 are correct, and there are no cross-reactivities with other high-risk human papillomavirus.

2. Specificity

Please see the cross-reactivities and its verified concentration level of verified other HPV genotypes and related pathogens in the table below:

Microorganism Name	Cross-reaction Concentration	Microorganism Name	Cross-reaction Concentration
Related Pathogens			
Chlamydia trachomatis	1.00E+06 CFU/mL	*Ureaplasma urealyticum*	1.00E+06 CFU/mL
Neisseria gonorrhoeae	1.00E+06 CFU/mL	*Trichomonas vaginalis*	1.00E+06 cells/mL
Mycoplasma hominis	1.00E+06 CFU/mL	*Treponema pallidum*	1.00E+06 copies/mL
Candida albicans	1.00E+06 CFU/mL	Herpes simplex virus type 2	5.00E+06 copies/mL
Human papillomovirus out of the detection scope of this diagnostic kit			
HPV6	1.00E+06 copies/mL	HPV11	1.00E+06 copies/mL
HPV26	1.00E+06 copies/mL	HPV40	1.00E+06 copies/mL
HPV42	1.00E+06 copies/mL	HPV43	1.00E+06 copies/mL
HPV44	1.00E+06 copies/mL	HPV54	1.00E+06 copies/mL
HPV61	1.00E+06 copies/mL	HPV67	1.00E+06 copies/mL
HPV69	1.00E+06 copies/mL	HPV70	1.00E+06 copies/mL
HPV71	1.00E+06 copies/mL	HPV72	1.00E+06 copies/mL
HPV73	1.00E+06 copies/mL	HPV81	1.00E+06 copies/mL
HPV82	1.00E+06 copies/mL	HPV83	1.00E+06 copies/mL

3. Precision

A precision study was carried out, which was tested twice per day on three lots of reagents by two different operators for 21 days. The test numbers of every sample is 84 (21 days, twice per day, two repetitions for every test). Within-run, between-run, between-lot, between-day, between-operator and %CV for total Ct value were less than 5%.

4. Limit of Detection

Prepare a series of diluted samples to evaluate the lowest limit of detection for every different genotype of HPV DNA, and use 100% positive detection concentration level as the standard to determine the lowest limit of detection. The lowest limit of detection of every genotype is 1000 copies/mL.

5. Interfering substances

The concentration level and interference situations of the verified interfering substances are as below.

Interfering substances	Concentration level	Whether interference exists (yes or no)
hemoglobin	2 g/L	No
white blood cell	1.00E+07 cells/mL	No
cervical mucus	10%	No
contraceptive gel	0.5%	No
vaginal douche	0.5%	No
antifungal ointment, containing 2% Clotrimazole	0.5%	No
antifungal ointment, containing 2% Miconazole	0.5%	No
vaginal lubricant	10%	No

List of references

1.Bønløkke S, Stougaard M, Sorensen BS, et al. The Diagnostic Value of Circulating Cell-Free HPV DNA in Plasma from Cervical Cancer Patients. Cells. 2022; 11(14).
2.Desai KT, Adepiti CA, Schiffman M, et al. Redesign of a rapid, low-cost HPV typing assay to support risk-based cervical screening and management. International Journal of Cancer. 2022.
3.Wotman M, Ferrandino R, Gold B, et al. High-risk non-16 human papillomavirus genotypes in head and neck squamous cell carcinoma. Journal of Clinical Oncology. 2022; 40(16_suppl): e18052-e18052.
4.Santella B, Schettino MT, Franci G, et al. Microbiota and HPV: The role of viral infection on vaginal microbiota. Journal of Medical Virology. 2022; 94(9):4478-4484.

Symbol key

Symbols	Meanings	Symbols	Meanings
IVD	*In Vitro* Diagnostic Medical Device		Date of Manufacture
	Use-by date		Consult instructions for use
	Temperature Limit		Manufacturer
LOT	Batch Code	REF	Reference Number
Σ	Contains sufficient for <n> tests		Caution
CONTROL -	Negative Control	CONTROL +	Positive Control
ENZYME MIX	Enzyme Mix	PCR MIX	PCR Mix
PRE	Prepackaging	VERSION	Version
PAP 21	PAP21: Not corrugated cardboard		Keep away from light
	Do not re-use	UDI	Unique device identifier
EC REP	Authorized representative in the European Community	CE	This product fulfills the requirements of the European Directive 98/79/EC for *in vitro* diagnostic medical devices.

Contact information

Sansure Biotech Inc.
Add.: No. 680, Lusong Road, Yuelu District, 410205 Changsha, Hunan Province, PEOPLE'S REPUBLIC OF CHINA
Tel.: +86-731-88883176
Fax: +86-731-88884876
Web: www.sansureglobal.com

Obelis s.a.
Bd. Général Wahis 53, 1030 Brussels, BELGIUM
Tel.: + (32) 2.732.59.54
Fax: + (32) 2.732.60.03
E-Mail: mail@obelis.net