Instructions for Use of High Risk HPV DNA Test (PCR Fluorescent Probe Method)

G (2013) 002

Controlled Version: V1.4, Controlled Date: June 14, 2022

1. Name
High Risk HPV DNA Test (PCR Fluorescent Probe Method)

2. Serial Number of Kit
G (2013) 002

3. Specification
24 tests/kit

4. Shelf life
9 months at 2ºC-30ºC.

5. Intended Use
This kit is suitable for the qualitative detection of 18 high-risk genotypes of HPV (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82) that could cause the cervical cancer in cervical exfoliated cell and genitourinary tract secretion, which could specifically detect and distinguish HPV type 16 and type 18 with a higher rate of incidence. The result is for information only, should not be a base of making a final diagnosis or depleting cases.

6. Principle
PCR technique for diagnosis of pathogen is based on the amplification of special fragment of genome from the pathogen. Different from classical PCR techniques, fluorescent PCR uses fluorochrome to directly reflect the quantity change of PCR amplified products via changes of fluorescence energy released by excitation light stimulation. Variant of fluorescent signal is directly proportional to that of the amplified product. Collection and analysis of fluorescence is realized by highly sensitive automatic instrument so that original template quantity can be quantified. The kit adopts composite probe technique. Complex gene probes is named double-strand oligonucleotide, consisting of two complementary strands. The long strand has its reporter gene marked by fluorescent probe at 5' end and 3' end phosphorylated, and the short strand has its quenching gene marked by quenching probe. The quenching probe can hybridize with the 5' end of fluorescent probe. During the annealing step without template, the long probe combines the short probe and forms a double strand, so the quencher TAMRE inhibits the fluorescence emission from the reporter FAM. When a template exists in the reaction system, the combination between template and the long probe is stronger than combination between the short probe and template. The template has an advantage to interact with the long probe, so the short probe only can combine with the other template. Therefore, the two probes are apart and target the two DNA complementary strands respectively. The fluorescence now can be captured, and the signals increase. In the following elongation phase of PCR, when the DNA prolong to the position of the probes, Taq DNA polymerase digests the inhibitive probes into single nucleotides by its 5'-3' exonuclease activity, and helps to continue the process of prolongation of the DNA strands. Accordingly, PCR quantification determination can be performed. The common experimental instruments are real-time fluorescent detection instruments such as ABI 7500. The quantification result can be gotten directly by computer analysis when the reaction is over.

7. Product Description
High Risk HPV DNA Test (PCR Fluorescent Probe Method) applies to qualitative in vitro diagnosis of High Risk HPV in the samples. This diagnostic method is based on PCR technique, combined with composite probe technique, which can realize rapid auxiliary diagnosis of High Risk HPV infection.
Detailed clinical study validates high specificity, sensitivity, and reproducibility of the kit, which can be used for early diagnosis of clinical infection of High Risk HPV. See relevant information in 17. Technological Specification.

8. Contents

Name	Content
DNA extracting reagent	·1 × 1200µl ·Tris-HCl,EDTA
HPV PCR reaction tube	·24 tubes ·Upstream primer and downstream primer ·Fluorescent probe ·Hot Start Taq DNA polymerase, UNG, dNTPs
Rehydration Solution	·1 × 960 µl ·Tris-HCl, $(NH_4)_2SO_4$, KCl_2, Mg^{2+}
Negative control	·1 × 100 µl ·Purified water
HPV positive control	·1 × 100 µl ·Hela cells
Instructions for Use	·1 copy

9. Applicable Instruments
ABI PRISM® 7500 SDS
There are many kinds of real-time PCR apparatus except we used, including ABI7900 (Applied Biosystems), MX4000 (Stratagene), iCycler (Bio-Rad), Smartcycler (Cepheid), Robocycler (MJ Research), RotorGene (Corbett), Hangzhou Bori (Linegene). Different apparatus have different using method, but each have the detecting ability for Taqman probe and Sybrgreen dyeing. It's necessary to estimate the compatibility between those apparatus and High Risk HPV fluorescent PCR kit produced by the company.

10. Warnings and Precautions
10.1 Users should read the instruction carefully.
10.2 For in vitro diagnostic use only.
10.3 Do not pipet by mouth.
10.4 Do not eat, drink, or smoke in laboratory working area. Wear protective disposable glove, laboratory coats, and eye protection when handling specimens and kit reagents. Wash hands thoroughly after handling specimens and reagents.
10.5 Avoid microbial contamination of reagents when removing aliquots from reagent bottles. The use of disposable pipet tips is recommended.
10.6 Do not reverse the reagent.
10.7 Dispose of unused reagents and waste in accordance with country, federal, state, and local regulations.
10.8 Do not use a kit after its expiration date.
10.9 Workflow in the laboratory must proceed in a unidirectional manner, beginning in the Pre-Amplification area and moving to the Post-Amplification (Amplification/Detection) area. Pre-amplification activities must begin with reagent preparation and proceed to specimen preparation. Supplies and equipment must be dedicated to each pre-amplification activity and not used for other activities or moved between areas. Gloves must be worn in each area and must be changed before leaving that area. Equipment and supplies used for reagent preparation must not be used for specimen preparation activities or for pipetting or processing amplified DNA or DNA extraction buffer. Post-amplification supplies and equipment must remain to the Post-amplification area at all times.
10.10 Specimens should be regarded as infectious and processed in accordance with safe laboratory procedures required in country, federal, state, and local regulations. Thoroughly clean and disinfect all work surfaces with 10% bleaching solution. Supplies and equipment that have contacted specimens must be processed with high pressure before being discarded.
10.11 This detection only applies to cervical exfoliated cell and genitourinary tract secretion samples.

11. Stability and Storage
11.1 Properties of all the components of the kit are stable during transport under low temperature with dry ice or ice bag in a stable temperature: 2ºC~30ºC
11.2 After receiving the kits, open the outer packaging carton to validate the temperature ≤ 30º C, which can demonstrate that the quality of the reagents is not influenced during transport. Otherwise, please contact the manufacturing company or the agent in European Union to change the kits.
11.3 When getting the new kits, please immediately store them at 2º C~30º C.
11.4 The kit is stable until expiry date when operating according to the Instruction for Use.
11.5 The rest kit after opened should be stored at 2º C~30º C, and it is stable until the expiry date.

12. Materials and instruments required but not provided
·Stroke-physiological saline solution
·Disposable gloves and masque, powderless
·1.5ml centrifuge tube and 0.5ml centrifuge tube
·Vortex mixer
·Adjustable pipettes and pipette tips with filters
·Table model high speed centrifuge with rotor for 1.5ml reaction tube
·Thermostat-controlled waterbath or other thermostatic equipment
·Real-time PCR amplification apparatus
·Specific reaction tube for PCR amplification apparatus (0.2ml light reaction tube and glass capillary)
·Ice
·Deionized water

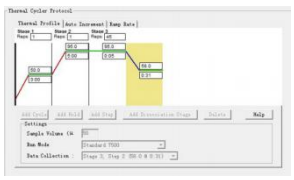
13. Pathogen Information
Cervical cancer is one of the most common female malignancies, which is mainly caused by the persistent infection or repeated infection of high-risk HPV. Therefore, HPV DNA detection has been regarded as an important part of cervical cancer screening and health management in a number of countries around the world. HPV has numerous genotypes, which could be classified as low-risk type and moderately high risk type. The main significance for HPV DNA detection is: (1) to decide if the further vaginoscopy is needed for patient based on the liquid based cytology detection result; (2) to take the follow-up visit for the patients with abnormal LBC result but negative colposcopy or biopsy result; (3) to make the prognosis of clinical treatment for the patients with high-grade cervical intraepithelial neoplasia; (4) to perform the early screening of cervical cancer by combining with pap smear for those women above 30 years old.
This kit utilizes 4 fluorescence indicators, of which HEX labels the probe for common high-risk HPV type 16, TEXRD labels the probe for common high-risk HPV type 18, FAM labels the probe for other 16 types of HPV genotype (26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82) , and CY5 labels the probe for internal control gene, thus to realize the simultaneous detection for 18 genotypes of HPV in the same tube.

14. Specimen Type, Collection, Pre-treatment, Transport, and Storage
14.1 Applicable specimens: cervical exfoliated cell and genitourinary tract secretion.
14.2 Specimen Collection
⚠**Note:** All specimens have to be treated as potentially infectious material.
Wash the sampling part with sterilized normal saline, and then use the epithelial brush (the cervical brush, swab etc.) to collect the exfoliated cell, focus epithelial cell and secretion etc. of cervix or genitourinary tract, put the epithelial brush with sample (cervical brush, swab etc.) into the sterilized preservative tube, seal up and submit it for detection. Label the tube with patient information and date/time collected.
14.3 Specimen transport
In order to ensure high quality of the specimens for laboratory use, specimens should be transported to laboratory as soon as possible. Specimens should be transported at controlled temperature.
14.3.1 Specimens may be transported to the test site at 18-25°C provided that the total time of storage and transport at 18-25°C is less than 1 hour. Refrigerate specimens if transport to the laboratory is delayed for more than one hour from the time of collection.
14.3.2 Transportation of specimens must comply with country and local regulations for the transport of etiologic agents.
14.4 Specimen storage
Note: Routine freezing or prolonged storage of specimens may affect performance.
The sample could be sent for detection immediately or preserved at 4-8ºC (2 weeks); or immerse the epithelial brush into cell preservative solution (the cell preservative solution produced by GuangZhou Heas BioTech Co., Ltd. is recommended) or put the cells in preservative solution, the storage condition and duration could refer to the instruction of cell preservative solution, and the preservative solution should be discarded by centrifugation before using the sample.

15. Test Procedure
15.1 DNA extraction
15.1.1 Specimen processing
15.1.1.1 Shake the preservative tube containing cervical brush for 10-30 seconds (make the cells fully drop into the solution), and pipette 0.5-1.0 ml of cervical exfoliated cell sample (the sample volume could be added to 2.0 ml in case of few cells) into a 1.5 ml centrifuge tube.
15.1.1.2 Centrifuge at 10,000 rpm for 3 minutes, and remove the supernatant and discard.
15.1.1.3 Add 1 ml of sterilized normal saline to the sediment, wash the sediment, centrifuge at 10,000 rpm for 3 minutes, and remove the supernatant and discard.
15.1.1.4 Add 50 µl of DNA extracting reagent to the sediment, shake for 60 seconds to fully suspend the cell sediment, 100℃ 10min，centrifuge at 10,000 rpm for 3 minutes，and reserved for further use.
15.1.2 Quality control processing
15.1.2.1 Take out HPV positive control and negative control, transfer the HPV positive control and negative control to 1.5ml EP tube, add 1 ml of sterilized normal saline to the sediment, wash the sediment, centrifuge at 10, 000 rpm for 3 minutes, and remove the supernatant and discard.
15.1.2.2 Add 50 µl of DNA extracting reagent to the sediment and shake for 60 seconds, fully suspend the cell sediment,100℃ 10min，centrifuge at 10,000 rpm for 3 minutes，and reserved for further use.
⚠Commercially available DNA extraction buffer kits can also be used for DNA extraction. The extracted DNA can be directly used for the kit, or can be stored for one year at a temperature at -20ºC±5ºC, but repeated freezing and thawing should be avoided.
15.2 PCR amplification
15.2.1 Sampling
Add 40 µl Rehydration Solution and 5 µl extracted DNA from samples to each reaction tube (including negative control, sample, and positive control). Cap the tubes tightly and vortex at least 10 second until the glass powder is completely dissolved, gently swing the tubes to make the liquid gather at the bottom.
During the whole process of application of sample, the samples should be applied in the following order: first negative control, second detection sample, last positive control. After application of sample, all PCR reaction tubes should be enclosed, avoiding cross contamination.
15.2.2 Programming ABI PRIM® 7500 Sequence Detection Systems
15.2.2.1 Procedure setup (See detailed information in operation manual of each instrument.)
15.2.2.1.1 Open the "Setup" window, and set the negative control (NTC), positive control and the unknown samples (Unknown) in sequential according to the samples arrangement. Then input the sample name in the "Sample Name" column and set the "Probe Mode" as follow:

Target	Detector Name	Reporter Dye	Quencher Dye
16 common high-risk genotypes of HPV (26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58 ,59, 66, 68, 73, 82)	FAM	FAM	NONE
HPV16	HEX	VIC/HEX	NONE
HPV18	TEXRD	TEXAS RED/ROX	NONE
Internal control gene (PPIA)	CY5	CY5	NONE
/	/	Passive Reference	NONE

15.2.2.1.2 Open the instrument window to set up the circulation program:
Set up the detection time and temperature, according to the following three stages (See Figure 2). If further information is needed, please look up in Chapter 4 of Applied Biosystems 7500 Real-Time PCR System Absolute Quantification Getting Started Guide.
Figure 2 Setup of detection time and temperature



Detection Temperature and Time		
	Number of cycle	Temperature and Time
Stage1	1	50.0ºC, 3:00
Stage2	1	95.0ºC, 5:00
Stage3	45	95.0ºC, 0:05; 58.0ºC, 0:31

15.2.2.2 Data analysis
15.2.2.2.1 Setup of analysis condition (If further information is needed, please look up in Chapter 6 of Applied Biosystems 7500 Real-Time PCR System Absolute Quantification Getting Started Guide):
Automatically save the results after the reaction is completed. Regulate appropriate Baseline and Threshold according to the picture after analysis (Users can adjust these according to their own situations. For the Start value is usually set between 3 and 15, and the End value is usually between 5 and 20. Set the Value of Threshold in Log graph window to put the threshold line at the logarithmic phase of amplification curve, and the amplification curve of negative control should be smooth straight or lower than the threshold line). It is suggested that the threshold line is adjusted to 1/20 of maximum fluorescence value in each channel, for example, if four channels are requested for the kit, we need to respectively adjust the threshold line of FAM, HEX, TEXRD and CY5 channel to 1/20 maximum fluorescence value of each channel. Click "Analysis" that automatically releases the analytical result and record the Ct value of the specimen.

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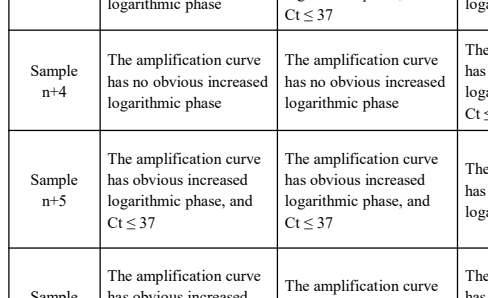
15.2.2.2.2 Result interpretation

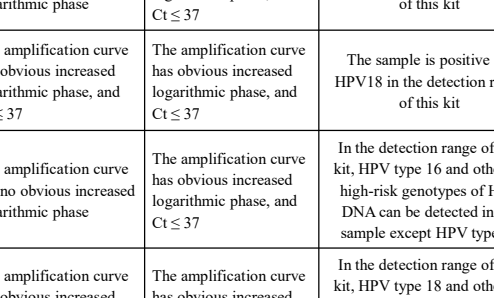
Sample name	FAM channel	HEX channel	TEXRD channel	CY5 channel	Result interpretation
Sample n	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The sample is negative in the detection range of this kit
Sample n+1	The amplification curve has no obvious increased logarithmic phase, but Ct ≤ 37	The amplification curve has no obvious increased logarithmic phase, but Ct ≤ 37	The amplification curve has no obvious increased logarithmic phase, but Ct ≤ 37	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The sample is negative in the detection range of this kit
Sample n+2	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	In the detection range of this kit, the other 16 high-risk genotypes of HPV are positive except type 16 and type 18
Sample n+3	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The sample is positive for HPV16 in the detection range of this kit
Sample n+4	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The sample is positive for HPV18 in the detection range of this kit
Sample n+5	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	In the detection range of this kit, HPV type 16 and other 16 high-risk genotypes of HPV DNA can be detected in the sample except HPV type 18
Sample n+6	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	In the detection range of this kit, HPV type 18 and other 16 high-risk genotypes of HPV DNA can be detected in the sample except HPV type 16
Sample n+7	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 33	The amplification curve has no obvious increased logarithmic phase	In the detection range of this kit, HPV type 18 DNA can be detected in the sample (In case of large viral load and few cell nuclei when sampling)
Sample n+8	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 33	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	In the detection range of this kit, HPV type 16 DNA can be detected in the sample (In case of large viral load and few cell nuclei when sampling)
Sample n+9	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, but Ct > 37	The amplification curve has obvious increased logarithmic phase, but Ct > 37	The concentration of sampling is less than the detection sensitivity of this kit. The sample is negative in the detection range of this kit. It is recommended to re-extract the HR-HPV DNA
Sample n+10	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The internal control gene can not be detected, please re-prepare the sample to test again
Sample n+11	Any other phenomenon appears except for the situation mentioned above	Any other phenomenon appears except for the situation mentioned above	Any other phenomenon appears except for the situation mentioned above	Any other phenomenon appears except for the situation mentioned above	Please test again or kindly go to consult the technician

The positive detection result in the detection range of this kit is showed as follow:

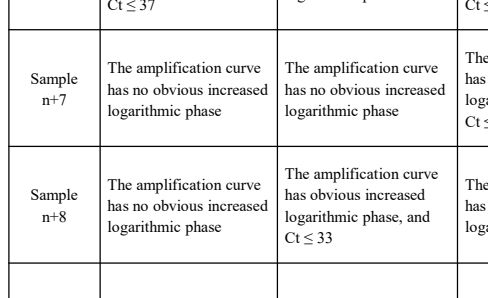
HPV type 16



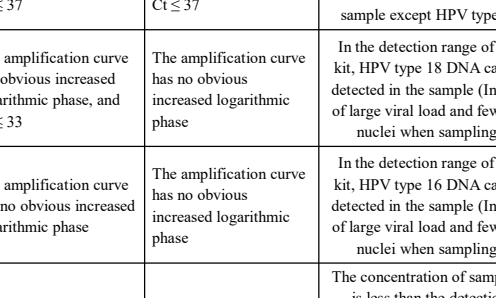
HPV type 18



HPV type 26



Negative sample



16. Quality Control

Sample name	FAM channel	HEX channel	TEXRD channel	CY5 channel	Result
Negative control	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	Negative
Positive control	The amplification curve has no obvious increased logarithmic phase	The amplification curve has no obvious increased logarithmic phase	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	The amplification curve has obvious increased logarithmic phase, and Ct ≤ 37	Positive

⚠**Note:** The above requirements should be met in the same experiment, otherwise, the experiment is invalid and it should be re-performed.
⚠**Note:** Perform quality control for each experiment.

17. Technological specification

17.1 Sensitivity: the analytical sensitivity of ABI PRISM® 7500 SDS is 5.0×10^3 copies/ml by laboratory evaluation; diagnostic sensitivity is 100% for use with ABI PRISM® 7500 SDS by clinical study evaluation.
17.2 Specificity: the analytical specificity of ABI PRISM® 7500 SDS is 100% by laboratory evaluation; diagnostic specificity is 92.82% for use with ABI PRISM® 7500 SDS by clinical investigation evaluation.
17.3 Precision:
Precision of kit when tested in ABI PRIM® 7500 Sequence Detection Systems

Sample concentration	$5{,}0\times10^5$ cópias/ml	
	HEX	CY5
Within run SD	0.55	0.58
Within run CV	2.58%	2.34%
Between run SD	0.55	0.80
Between run CV	2.60%	3.30%

17.4 Stability: Result of experimental study on stability shows that the High Risk HPV DNA Test (PCR Fluorescent Probe Method) can be stored for 9 months at 2ºC-30ºC. Perform acceleration testing at 37°C for 60 hours, and does not affect the performance of the kit.

18. Product Use Limitations

18.1 Polymerase repression may result in fault negative result.
18.2 Reliable results depend on correct specimen collection and transport.
18.3 Detection of High Risk HPV depends on quantity of microorganism contained in the specimen, and is influenced by collection methods, patient factors (for example, age and forthcoming symptoms), and infection.
18.4 The kit only applies to specified specimen types. Detection of other types may result in false positive or false negative results.
18.5 The kit can not be used to assess a treatment.
18.6 Like other diagnostic experiments, all clinical and laboratory results should be considered and then an interpretation can be made.
18.7 The product is to be used by personnel specially trained on PCR technique only.

19. Troubleshooting

19.1 No fluorescent increase signal in reaction tube of positive control
• Procedure setup error
Check according to 15.2.3.1 in the Instructions for Use.
• Preparation error of PCR reaction system
Check one by one according to preparation table, when necessary, repeat PCR reaction.
• Use kit after its expiration date or use deteriorated reagent
Check the storage condition of the kit prior to use and use the reagents during its shelf life. Store reagents according to the storage condition specified in the Instructions for Use.
19.2 Fluorescent increase signal emerges in reaction tube of negative control
19.2.1 Contamination occurs in experiment
◆Laboratory management should be strictly performed according to management specification for PCR gene amplification laboratory. The experimenters should receive special training. The experiment should be strictly processed in separate areas (reagent preparation area, specimen preparation area, amplification area and amplicon analysis area). All consumables used should be single-use. Each stage of the experiment should apply special apparatus and equipment, and cross-use should be avoided between different areas and different stages.
◆Repeat the experiment using new reagents.
◆During application of samples, keep to the following order: first negative control, second detection sample, last positive control. After application of sample, all PCR reaction tubes should be enclosed.
If there are other problems, please contact our technique supporters. Email xxw@heasbio.com

20. Manufacturer

GuangZhou Heas BioTech Co., Ltd.
Manufacturing Address: 6F, 7F, Building C5 and 3F, Building B10 and 4F, Building A8, No. 11, Kaiyuan Road, High-Tech Industrial Development District, Guangzhou, Guangdong, 510530, P.R. China
Tel: +86-20-89852732
Website：http://www.hasbio.com

21. Reference standard

ISO 15223-1:2012 Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
BS EN ISO 18113-3:2011 In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 3: In vitro diagnostic instruments for professional use
BS EN ISO 18113-2:2011 In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use

22. Reference

• Wright TC Jr, Schiffman M. Adding a test for human papillomavirus DNA to cervical-cancer screening. N Engl J Med. 2003; 348: 489-490.
• Muñoz N, Bosch FX, de Sanjose S, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med. 2003; 348 (6): 518-527.
• Unger ER, Dillner J, editors. Human Papillomavirus Laboratory Manual. 1st Edition Geneva: World Health Organization; 2009.
• Bouvard V, Baan R, Straif K, et al. A review of human carcinogens - Part B: biological agents. Lancet Oncol. 2009; 10: 321-322.
• Castle PE, Schiffman M, Wheeler CM, et al. Impact of improved classification on the association of human papillomavirus with cervical precancer. Am J Epidemiol. 2010; 171: 155-163.
• De Sanjose S, Quint WG, Alemany L et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. Lancet Oncol. 2010; 11 (11): 1048-1056.
• Katki HA, Kinney WK, Fetterman B, et al. Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: a population-based study in routine clinical practice. Lancet Oncol. 2011; 12 (7): 663-672.
• Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin. 2012; 62 (3): 147-172.

23. European Authorised Representative

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Email: office@kingsmead-service.com

24. Explanation of Symbols

	Use by	REF	Catalogue number	IVD	In vitro diagnostic medical device
LOT	Batch code		Temperature limitation	CE	CE marking
	Manufacturer	Σ	Contains sufficient for <n> tests		Warning sign
EC REP	European Authorised Representative		Consult Instructions For Use		Do not reuse.