STANDARD M10 HPV

STANDARD™ M10 HPV

REF M10-HPV-01

INSTRUCTIONS FOR USE

For use with STANDARD™ M10 system

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SD BIOSENSOR

Contents

1. Intended Use

The STANDARD M10 HPV test is a multiplex real-time PCR test intended for use with STANDARD M10 system for the qualitative detection of Human papillomavirus (HPV) DNA in cervical swab collected from individuals suspected of HPV infection by their healthcare provider.
The STANDARD M10 HPV separately detects genotypes 16, 18 and reports 12 high-risk HPV types (i.e., 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) in a pooled result.
Results are for the identification of 14 high-risk HPV DNA. Positive results are indicative of the presence of HPV DNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status.
The STANDARD M10 HPV can assess the presence or absence of HPV genotypes 16, 18 and 12 high-risk HPV types.
Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.
Negative results do not preclude HPV infection and should not be used as the sole basis for treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.
The STANDARD M10 HPV test is intended to be performed by trained users in both laboratory and near-patient testing settings.

2. Summary and Explanation

HPV infection is caused by human papillomavirus, a DNA virus from the *Papillomaviridae* family. HPV are transmitted by skin-to-skin contact and sexual contact. HPV infection results in either warts or precancerous lesions. These lesions increase the risk of cancer of the cervix, vulva, vagina, penis, anus, mouth.
Human papillomavirus is small double-stranded circular DNA virus. The circular genome is approximately 7.9 kb. Currently, there are more than 100 different known HPV genotypes that have been grouped into low-risk and high-risk categories. Nearly all cervical cancer is due to HPV; two strains, HPV 16, and HPV 18, account for 70% of cases.
The STANDARD M10 HPV test is a molecular *in vitro* diagnostic test that aids in the detection and diagnosis of HPV and is based on widely used nucleic acid amplification technology. The STANDARD M10 HPV test contains primers and probes and internal control (IC) used in Real-time PCR for the *in vitro* qualitative detection of HPV DNA in cervical swab specimens.

[Cartridge Description]
The STANDARD M10 HPV cartridge is a disposable plastic device that allows performance of fully automated molecular assays by containing all reagents required for the test.
Within the cartridge, multiple steps are automatically performed in sequence using pneumatic pressure to transfer samples and fluids via the chamber to their intended destinations.

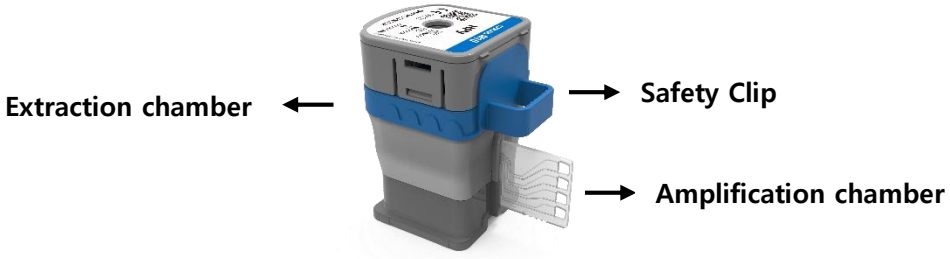

Figure 1. Layout of the STANDARD M10 HPV cartridge

3. Principle of the Procedure

The STANDARD M10 HPV test is an automated *in vitro* diagnostic test for qualitative detection of nucleic acid from HPV. The STANDARD M10 HPV test is performed on STANDARD M10 system.
The STANDARD M10 system automates and integrates sample preparation, nucleic acid extraction and, real-time polymerase chain reaction (qPCR), and detection of the target sequences in various specimens using molecular diagnostic assays. The system consists of the STANDARD M10 Module and the STANDARD M10 Console with preloaded software for running tests and viewing the results. The system requires the use of single-use disposable cartridges that hold the qPCR reagents and host the qPCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, see the STANDARD M10 system User Manual.
The STANDARD M10 HPV test includes reagents for the detection of DNA from HPV in cervical cells. The cartridge is present to control for adequate processing of the sample and qPCR reaction.
The table below indicates which target is designed to be detected by which channel.
The STANDARD M10 HPV separately detects results as follows : “HPV 16”; for HPV 16, “HPV 18”; for HPV 18, “G1” for the result of HPV types 51, “G2” for the pooled result of any of HPV types 33, 52, 58, “G3” For the pooled result of either of HPV types 31 or 35, “G4” for the pooled result of either of HPV types 45 or 59, “G5” for the pooled result of either of HPV types 39, 68, “G6” for the pooled result of either of HPV types 56 or 66.

Table 1. Fluorescent channel of each target gene

Target	Channel	Notation
HPV 16	FAM	HPV 16
HPV 18	FAM	HPV 18
HPV 51	FAM	G1
HPV 33, 52, 58	CY5	G2
HPV 31, 35	FAM	G3
HPV 45, 59	CY5	G4
HPV 39, 68	CY5	G5
HPV 56, 66	CY5	G6
Internal control (IC)	HEX	IC

4. Materials Provided

The STANDARD M10 HPV contains sufficient reagents to process 10 specimens or quality control samples.

Table 2. Contents of the STANDARD M10 HPV kit

	Contents	Quantity	Usage in each reaction
1	Cartridge	10	1ea
2	Quick Reference Instructions	1	-

5. Storage and Handling

Store the STANDARD M10 HPV kit at 2 - 28°C (36 - 82°F). If the cartridge has been refrigerated, perform the test after stabilizing it for 30 minutes at room temperature (20 - 28°C, 68 - 82°F). Do not remove the safety clip of the cartridge and do not press the cartridge until actual use. This kit should be stored at appropriate temperature and kept away from UV/sunlight. Do not use a cartridge that has leaked or is wet. Under these conditions, cartridges can be stored until the expiration date printed on the packaging.

6. Materials Required but Not Provided

- STANDARD M10 system with user manual
  At least one STANDARD M10 Console (Cat. No. 11M1011) and one STANDARD M10 Module (Cat. No. 11M1012)
- Vortex mixer
- Sample collection tools
  - Chlamydial Transport Media (Asan Pharmaceutical Co., LTD, AM608-02)
  - Cervix-Swab™ STD/HPV Swab collection kit (Noble Bioscience)
- STANDARD M10 STI Sample Pretreatment Kit (SD Biosensor, Cat. No. 11PRT30A)
- PPE (Personal Protective Equipment)

7. Warnings and Precautions

1) This kit is only for *in vitro diagnosis*.
2) For professionals use only.
3) Please read the Instructions for Use carefully before testing.
4) Improper specimen collection, transfer, storage, and processing may cause erroneous test results.
5) Do not remove the safety clip of the cartridge before use.
6) Do not press the cartridge until actual use.
7) Do not use a cartridge that has leaked or is wet.
8) Keep the cartridge away from UV/sunlight and keep dry.
9) Do not use the kit after its expiration date.
10) Do not shake, tilt, or invert the cartridge especially after pressing the cartridge to punch the seal. It may yield invalid or false test results.
11) Do not use a cartridge with a damaged barcode label.
12) Do not reuse processed cartridges.
13) All patient samples should be handled as if these samples are infectious.
14) All materials should be considered potentially infectious and should be handled with precautions.
15) As this test involves extraction of viral DNA and PCR amplification, care should be taken to avoid contamination. Regular monitoring of laboratory contamination is recommended.
16) Clinical laboratories should be equipped with equipment and operators in strict accordance with the "Code of Practice for Clinical Gene Amplification Laboratories".
17) When using this kit, it should be operated strictly in accordance with the instructions and follow the technical requirements of the clinical gene amplification laboratory.

18) Follow your institution's environmental waste procedures for proper disposal of used cartridges.

8. Specimen Collection and Storage

Proper sample collection, transportation, and storage are critical to the performance of the test. Improper sample collection, inappropriate sample handling and/or transportation can lead to false results.

8.1 Specimen Collection

Collect cervical swab following your institution's standard protocol for sample collection and testing.

8.2 Specimen Storage and Transport

The swab specimens in the collection tube can be stored for 3 days at room temperature (19 ~ 25℃, 66 ~ 77˚F), for 5 days at refrigerated temperature(2 - 8℃, 36~46˚F), and for 8 weeks at -70℃(-94˚F).

9. Procedure

9.1 Starting the STANDARD M10 system

Note	For the detailed instructions, refer to the STANDARD M10 system user manual. If you have scanned the cartridge barcode in the STANDARD M10 and the software version is not compatible, a 'Not Supported Device' error message appears. Update the software before proceeding the test.

1) Turn on the STANDARD M10 system.
2) Check the STANDARD M10 Console and the STANDARD M10 Module are connected and functional.

Figure 2. Power connection

3) Enter the User ID and Password on the Log In screen of the STANDARD M10 Console and click the Log In button.
4) Touch the STANDARD M10 Module to run on the Home screen.
(The door of the selected STANDARD M10 Module will automatically open for cartridge loading.)

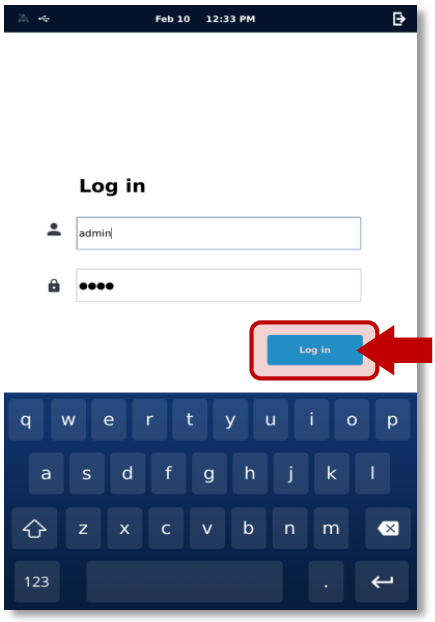

Figure 3. Log In screen

Figure 4. Home screen, Status of M10 Module

5) Enter a Patient ID by scanning the barcode or using virtual keyboard on the M10 Console screen.
(Patient ID is optional. You can turn off the Patient ID option from the 'Settings'.)
6) Enter a Sample ID by scanning the barcode of the specimen or using virtual keyboard on the M10 Console screen.
Make sure that the specimen tube cap is firmly closed when scan the ID barcode printed on the specimen tube.
(For quality control test, tick the QC check box.)

Figure 5. Entering Sample ID

Figure 6. Scanning a cartridge

7) Scan the STANDARD M10 HPV cartridge to be used. The STANDARD M10 Console automatically recognizes the assay to be run based on the cartridge barcode.

Note	If you have scanned the cartridge barcode in the STANDARD M10 and the expiration date has expired, An 'Expired Device' error message appears. Check validity period and test with unexpired cartridges.

9.2 Loading a sample into the STANDARD M10 HPV cartridge

Caution	If the cartridge has been refrigerated, perform the test after stabilizing it for 30 minutes at room temperature (20 ~ 28°C, 68 ~ 82°F). Once the sample has been loaded into the cartridge, start the test as soon as possible.
Note	False negative results may occur if insufficient sample is added into the cartridge.

1) Remove the safety clip located underneath the lid of the cartridge.
2) Pierce the sealed cartridge by pressing down the lid until fully engaged into the cartridge groove.

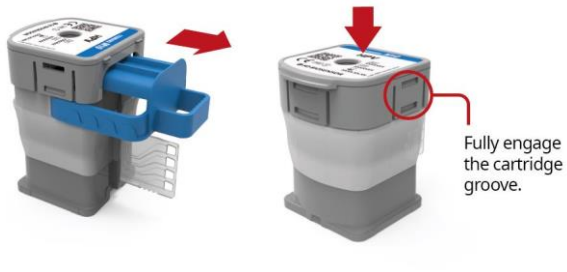

Figure 7. Pierce the sealed cartridge

3) Open the lid and check that the seal is completely punctured before loading a sample.
4) Vortex the prepared specimen vigorously for 10 seconds.
5) Insert the barrel tip of the STI Pretreatment tool into the sample hole of the cartridge.
6) Collect 1.4 ㎖ of the sample using the STANDARD Disposable dropper (1.4㎖) and transfer it to the barrel of the STI Pretreatment tool placed on the cartridge sample hole.
7) Load the entire sample into the cartridge by pushing the plunger of the STI Pretreatment tool.

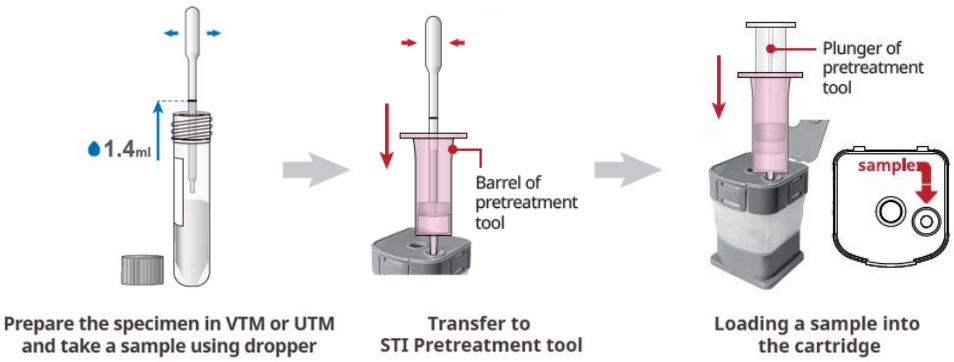

Figure 8. Loading a sample

8) After a few seconds, Sample Guide screen will automatically change to the Insert Cartridge screen. Touch the Sample Guide screen if you want to skip the guide.
9) Close the lid.

Figure 9. Sample Guide screen

Figure 10. Insert Cartridge screen

9.3 Running a test

1) Load the cartridge on the selected STANDARD M10 Module with the Amplification chamber facing the inside of the module. (The status indicator of the selected module will blink green.)
2) Close the door completely.
3) After confirming the sample and cartridge information, touch the OK button on the screen. (Touch the Reset button to re-input the information.)
4) Assay starts automatically, and remaining time will appear on the screen.

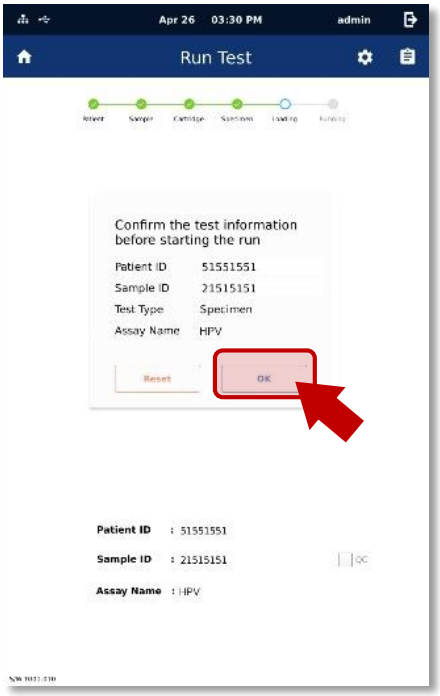

Figure 11. Confirm the test screen

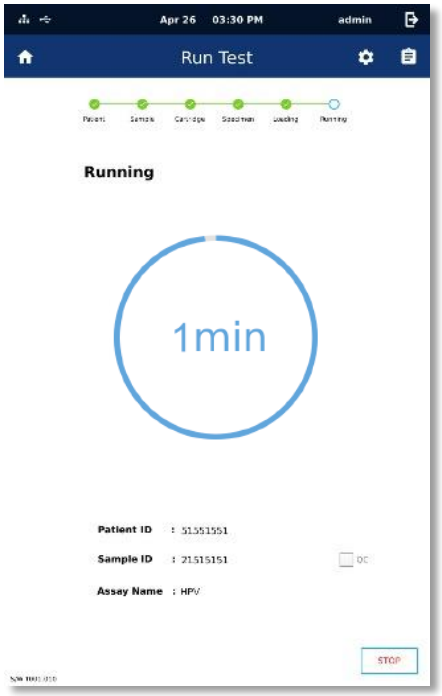

Figure 12. Running screen

5) When the run is finished, it switches to the Review screen and the result is displayed.
6) Dispose of used cartridges in the appropriate biohazard waste container according to your institution's standard practices.
7) To run another test, touch the Home icon and repeat the process.
(If another STANDARD M10 Module connected to the STANDARD M10 Console is available, you can start a new test while another test is running.)

10. Interpretation of Results

The results are interpreted automatically by the STANDARD M10 Console and are clearly shown in the Review screen. The STANDARD M10 HPV test provides test results based on the detection of targets according to the algorithms shown in Table 3.

Table 3. Interpretation of results

Outcome (Home screen)	Result (Review screen)	Description
Positive		At least one pathogen is positive.
Negative		No pathogen was detected.
Invalid		IC signal does not have a Ct value within the valid range.
Error		The test failed because either an error occurred or the test was canceled by the user.

Table 4. Description of IC results

Outcome (Summary screen)	Result (Summary screen)	Description
IC Valid		IC has a Ct within the valid range. : The test was completed. Report positive/negative results of target according to the interpretation shown in table 5.
IC Invalid		All pathogen are not detected and IC signal does not have Ct value within the valid range.
IC Error		The test failed because either an error occurred or the test was canceled by the user. Repeat the test.

Table 5. Interpretation of results

Result	HPV 16	HPV 18	HPV others	IC
HPV 16 Positive	+	-	-	+/-
HPV 18 Positive	-	+	-	+/-
Other high-risk HPV Positive	-	-	+	+/-
HPV 16 Negative; HPV 18 Negative; Other high-risk HPV Negative	-	-	-	+
Invalid	-	-	-	-
Error	No result			

Result	Interpretation
HPV 16 Positive	HPV16 viral DNA is detected. • The HPV 16 signal has a Ct within the valid range. • IC: N/A (not applicable); IC is ignored because each target amplification occurred.
HPV 18 Positive	HPV18 viral DNA is detected. • The HPV 18 signal has a Ct within the valid range. • IC: N/A (not applicable); IC is ignored because each target amplification occurred.

Other high-risk HPV Positive	Other high-risk HPV viral DNA is detected. • The other high-risk HPV signal has a Ct within the valid range. • IC: N/A (not applicable); IC is ignored because each target amplification occurred.
HPV 16 Negative; HPV 18 Negative; Other high-risk HPV Negative	HPV 16, HPV 18 and Other high-risk HPV target DNAs are not detected. • IC: Valid; IC has a Ct within the valid range.
Invalid	IC does not meet acceptance criteria and all targets are not detected. Repeat the test. • IC: Invalid; IC and viral DNA signals do not have a Ct within valid range.
Error	The test failed because either an error occurred or the test was canceled by the user. Presence or absence of target nucleic acids cannot be determined. Repeat the test.

Table 6. HPV Genotypes

Notation		HPV genotype
HPV 16		HPV 16
HPV 18		HPV 18
HPV Others	G1	HPV 51
	G2	HPV 33, 52, 58
	G3	HPV 31, 35
	G4	HPV 45, 59
	G5	HPV 39, 68
	G6	HPV 56, 66

11. Quality Control

STANDARD Quality Control procedures are intended to monitor cartridge and assay performance. If the controls are not valid, the patient results cannot be interpreted.

Internal control (IC): Ensures a proper sample has been applied, reagents in the cartridge are well functioning, there were no other interfering factors in the sample, and the procedure was performed correctly. In clinical samples showing positive signal for Human papillomavirus, the IC is reluctant and is ignored. If the IC fails where no Human papillomavirus are detected the result is invalid.

External controls should be performed in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's standard quality control procedures.

12. Performance

12.1. Limit of Detection Test

The analytical sensitivity of the STANDARD M10 HPV test was assessed with two lots of cartridges and using HPV positive cell lines (HPV 16 (SiHa), HPV 18 (HeLa S3)) and DNA plasmids of the 14 targeted high-risk HPV types. The standard materials were diluted into simulated negative cervical swab matrix.
The LoD for HPV positive cell lines and Plasmid DNA of the 14 HPV genotypes was estimated by running at least 5 serially diluted concentrations with 20 replicates for each concentration. Based on the test results, LoD was set through probit analysis.
The claimed LoD values for the tested genotypes are summarized in Table 7.

Table 7. Summary of the LoD test results

Type	Genotype	LoD	95% CI
HPV positive cell line	SiHa (HPV 16)	51 cell/mL	40.85~71.40 cell/mL
	HeLa S3 (HPV 18)	21 cell/mL	15.90~33.59 cell/mL
Synthesized HPV plasmid DNA	16	37 copies/test	28.76~53.55 copies/test
	18	46 copies/test	36.18~74.65 copies/test
	31	140 copies/test	107.31~240.86 copies/test
	33	83 copies/test	65.25~124.93 copies/test
	35	97 copies/test	78.23~138.35 copies/test
	39	82 copies/test	65.94~118.74 copies/test

	45	133 copies/test	104.58~207.85 copies/test
	51	131 copies/test	100.71~223.96 copies/test
	52	158 copies/test	125.41~238.34 copies/test
	56	126 copies/test	96.75~217.46 copies/test
	58	151 copies/test	116.23~252.25 copies/test
	59	54 copies/test	42.41~82.67 copies/test
	66	56 copies/test	44.57~84.16 copies/test
	68	139 copies/test	111.23~208.68 copies/test

12.2. Cross-Reactivity

The following 32 cross-reacting organisms, including sexually transmitted infections and reproductive tract infections that can be detected in cervical swab specimen and non-target HPV group (Low-risk HPV genotypes), were tested with STANDARD M10 HPV. In addition, the test is evaluated 14 genotypes of high-risk HPV (i.e. 16, 18 and 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68), which are the targets of STANDARD M10 HPV.

As a result, no cross-reactivity was observed for 32 organisms. For the remaining 14 cross-reacting organisms (i.e. 16, 18 and 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68), detection was confirmed for each target.

The organisms and test concentrations are listed in Table 8.

Table 8. Organisms and test concentration for cross-reactivity test

No.	Organism	Test concentration	Result
1	*Bacteriodes fragilis*	$1X10^6$ CFU/mL	No cross-reactivity
2	*Bifidobacterium adolescentis*	$1X10^6$ CFU/mL	No cross-reactivity
3	*Bifidobacterium breve*	$1X10^6$ CFU/mL	No cross-reactivity
4	*Candida albicans*	$1X10^6$ CFU/mL	No cross-reactivity
5	*Chlamydia trachomatis Serovar D*	$1X10^6$ IFU/mL	No cross-reactivity
6	*Clostridium perfringens*	$1X10^6$ IFU/mL	No cross-reactivity
7	*Corynebacterium xerosis*	$1X10^6$ CFU/mL	No cross-reactivity
8	*Enterobacter cloacae*	$1X10^6$ IFU/mL	No cross-reactivity
9	*Enterococcus faecalis*	$1X10^6$ CFU/mL	No cross-reactivity
10	*Escherichia coli*	$1X10^6$ CFU/mL	No cross-reactivity
11	*Fusobacterium nucleatum*	$1X10^6$ CFU/mL	No cross-reactivity
12	*Klebsiella pneumoniae*	$1X10^6$ IFU/mL	No cross-reactivity
13	*Lactobacillus acidophilus*	$1X10^6$ IFU/mL	No cross-reactivity
14	*Neisseria gonorrhoeae*	$1X10^6$ CFU/mL	No cross-reactivity
15	*Peptostreptococcus anaerobius*	$1X10^6$ IFU/mL	No cross-reactivity
16	*Proteus mirabilis*	$1X10^6$ CFU/mL	No cross-reactivity
17	*Proteus vulgaris*	$1X10^6$ CFU/mL	No cross-reactivity
18	*Pseudomonas aeruginosa*	$1X10^6$ CFU/mL	No cross-reactivity
19	*Staphylococcus aureus*	$1X10^6$ CFU/mL	No cross-reactivity
20	*Staphylococcus epidermidis*	$1X10^6$ CFU/mL	No cross-reactivity
21	*Streptococcus agalactiae*	$1X10^6$ CFU/mL	No cross-reactivity
22	*Streptococcus pyogenes*	$1X10^6$ CFU/mL	No cross-reactivity
23	*Trichomonas vaginalis*	$1X10^6$ Cell/mL	No cross-reactivity
24	*Mycoplasma homini*	$3X10^3$ CFU/mL	No cross-reactivity
25	*Ureaplasma urealyticum*	$1X10^6$ CCU/mL	No cross-reactivity
26	Human Adenovirus 40	$1X10^5$ PFU/mL	No cross-reactivity
27	Cytomegalovirus (CMV)	$1X10^5$ PFU/mL	No cross-reactivity

28	Epstein Barr virus (EBV)	$1X10^5$ copy/mL	No cross-reactivity
29	Herpes simplex virus 1 (HSV-1)	$1X10^5$ PFU/mL	No cross-reactivity
30	Herpes simplex virus 2 (HSV-2)	$1X10^5$ PFU/mL	No cross-reactivity
31	HPV 6	$1X10^5$ IU/mL	No cross-reactivity
32	HPV 11	$1X10^5$ IU/mL	No cross-reactivity
33	HPV 16	$2X10^6$ Copies/mL	Only HPV 16 detected
34	HPV 18	$2X10^6$ Copies/mL	Only HPV 18 detected
35	HPV 31	$8X10^6$ Copies/mL	Only G3 detected
36	HPV 33	$4X10^6$ Copies/mL	Only G2 detected
37	HPV 35	$5X10^6$ Copies/mL	Only G3 detected
38	HPV 39	$4X10^6$ Copies/mL	Only G5 detected
39	HPV 45	$7X10^6$ Copies/mL	Only G4 detected
40	HPV 51	$7X10^6$ Copies/mL	Only G1 detected
41	HPV 52	$9X10^6$ Copies/mL	Only G2 detected
42	HPV 56	$7X10^6$ Copies/mL	Only G6 detected
43	HPV 58	$8X10^6$ Copies/mL	Only G2 detected
44	HPV 59	$3X10^6$ Copies/mL	Only G4 detected
45	HPV 66	$3X10^6$ Copies/mL	Only G6 detected
46	HPV 68	$8X10^6$ Copies/mL	Only G5 detected

12.3. Interference

We confirmed no interference reactions for the following 13 interfering substances as follows: tested for negative specimen spiked with positive standard materials (HPV 16 and HPV 18) at 3xLoD, both with or without interfering substances.

Table 9. Potentially Interfering Substances

Type	No.	Factor	Substance	Final concentration
Exo-genous	1	Douche	Yeast Gard Douche	10% v/v
	2	Anti-fungal cream	Clotrimazole Vaginal Cream	0.25% w/v
	3		Vagisil Moisturizer	0.25% w/v
	4		Zovirax Cold Sore Cream	0.25% w/v
	5		Monistant1	0.25% w/v
	6		Norforms Feminine Deodorant Suppositories	10% w/v
	7	Vaginal lubricant	KY Jelly Personal Lubricant	10% w/v
	8	Lubricant	X3 Love gel	0.5% w/v
	9	Feminine spray	Summer's eve feminine spray	10% v/v
	10	Acetic acid	Glacial Acetic acid	5% v/v
Endo-genous	11	Others	Whole Blood	2% v/v
	12		Leukocytes	$1x10^6$ cells/mL
	13		Cervical mucus	5% v/v

12.4. Precision

1) Repeatability

Three concentrations of each of the two standard materials (HPV 16 and HPV 18) were repeated twice a day, 2 replicates per run using one lot for 12days.

As a result, within-Run, Between-Run, Between-Day, and Within-Laboratory satisfy the acceptance criteria with SD < 2.0 Ct, confirming repeatability.

Table 10. Summary of the repeatability test results

1) HPV 16

Concentration	Within-Run (Sr)	Between-Run (Srr)	Between-Day (Sdd)	Within-laboratory (ST)
3X LoD	0.46	0.22	0.18	0.54
1X LoD	0.79	0.46	0.06	0.92
0.1X LoD	-	-	0.48	-

2) HPV 18

Concentration	Within-Run (Sr)	Between-Run (Srr)	Between-Day (Sdd)	Within-laboratory (ST)
3X LoD	0.38	0.12	0.17	0.43
1X LoD	0.81	0.54	0.29	1.01
0.1X LoD	0.13	0.25	0.46	0.54

2) Reproducibility

Reproducibility was confirmed by repeating the test twice a day, 2 replicates per run for 5 days, by two operators at three sites with three lots using the same test concentration. In addition reproducibility was evaluated between-instrument by connecting 8 modules to one console and 1 module to 1 console.
As a result, it was confirmed that there was reproducibility by satisfying the acceptance criteria with SD < 2.0 Ct and CV < 5% in the evaluation between the following: operators and lots, sites and the instrument.

Table 11. Summary of the reproducibility test results

1) HPV 16

Concentration (copies/mL)	Between-site(%CV)	Between-instrument(%CV)	Between-Operator(%CV)	Between- lot(%CV)
3X LoD	2.60	2.60	2.21	2.34
1X LoD	2.41	3.02	2.91	2.60
0.1X LoD	2.04	1.62	2.07	2.59

2) HPV 18

Concentration (copies/mL)	Between-site(%CV)	Between-instrument(%CV)	Between-Operator(%CV)	Between- lot(%CV)
3X LoD	2.16	2.31	1.95	2.02
1X LoD	2.38	2.34	2.66	2.29
0.1X LoD	2.38	2.31	2.06	2.07

12.5. Clinical Trial

The test results of the STANDARD M10 HPV were compared with the confirmed results of HPV positive samples and HPV negative samples. The test was conducted using cervical swab specimen in VTM. Based on the clinical performance test, the clinical sensitivity and specificity are calculated as Table 12.

Table 12. Summary of Clinical Sensitivity and Specificity

Result		Confirmed		Total
		Positive	Negative	
STANDARD M10 HPV	Positive	25	0	25
	Negative	0	25	25
Total		25	25	50

-Clinical sensitivity: 100% (25/25, 95% CI: 86.28% to 100.00%)
-Clinical specificity: 100% (25/25, 95% CI: 86.28% to 100.00%)

13. Limitations

1) Performance characteristics of this test have been established with the specimen types listed in the Intended Use Section only. The performance of this assay with other specimen types or samples has not been evaluated.
2) A false negative result may occur if :
   - Sample concentrations is near or below the limit of detection of the test.
   - A specimen is improperly collected, transported or handled.
   - Inadequate numbers of organisms are present in the specimen.
   - Cartridges are exposed to improper environmental factors (temperature / humidity).
3) False positive results may happen from cross-contamination between patient samples, specimen mix-up and/or DNA contamination during product handling.
4) Qualitative detection of positive results in this kit does not indicate the presence of live virus. It is recommended to use other methods for confirmation at the same time.
5) This kit only classifies and identifies Human papilloma virus (HPV 16, 18 and 12 high-risk HPV types (i.e., 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68)). The test results are for clinical reference only. The clinical diagnosis and treatment of patients should be combined with their symptoms / signs, medical history, other laboratory tests and treatment responses considering.
6) Potential mutations within the target regions covered by the primer and/or probes of the test may result in failure to detect the presence of the pathogen.

14. References

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4) Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Munoz. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. Journal of Pathology. 1999; 189(1):12-19.
5) Clinical and Laboratory Standards Institute. 2008. Verification and Validation of Multiplex Nucleic Acid Assays: Approved Guideline. MM17-A. Clinical and Laboratory Standards Institute, Wayne PA.
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7) Khan MJ, Castle PE, Lorincz AT, Wacholder S, Sherman M, Scott DR, Rush BB, Glass, AG, Schiffman M. The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. Journal of the National Cancer Institute. 2005; 97(14):1072-79
8) FDA Guidance "Establishing the Performance Characteristics of In Vitro Diagnostic Devices for the Detection or Detection and Differentiation of Human Papillomaviruses

15. Symbols

	Reference number		Batch code
	*In vitro* diagnostic medical device		CE marking - European Conformity
	Consult Instructions for Use		Manufacturer
	Contains Sufficient for <n> Tests		Date of manufacture
	Caution		Authorized representative in the European Community
	Note		keep dry
	Do not re-use.		Keep away from sunlight
	Temperature limit		Do not use if packaging is damaged
	Use-by date		

For further information on

STANDARD M10
HPV

Please contact your
SD BIOSENSOR representative

Manufacturer
SD Biosensor, Inc.
Head office : C-4th&5th, 16, Deogyeong-daero 1556beon-gil, Yeongtong-gu, Suwon-si, Gyeonggi-do, 16690, REPUBLIC OF KOREA
Manufacturing site : 14, Jeungpyeongsandan-ro, Jeungpyeong-eup, Jeungpyeong-gun, Chungcheongbuk-do, 27915

EC REP Authorized Representative
MT Promedt Consulting GmbH
Ernst-Heckel-Straße 7 66386 St. Ingbert Germany
Phone : +49 6894 581020, Fax : +49 6894 581021

CE IVD

For *In Vitro* Diagnostic Use Only

Any inquiries regarding instructions provided should be addressed to: ts@sdbiosensor.com
or you can also contact us through www.sdbiosensor.com

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