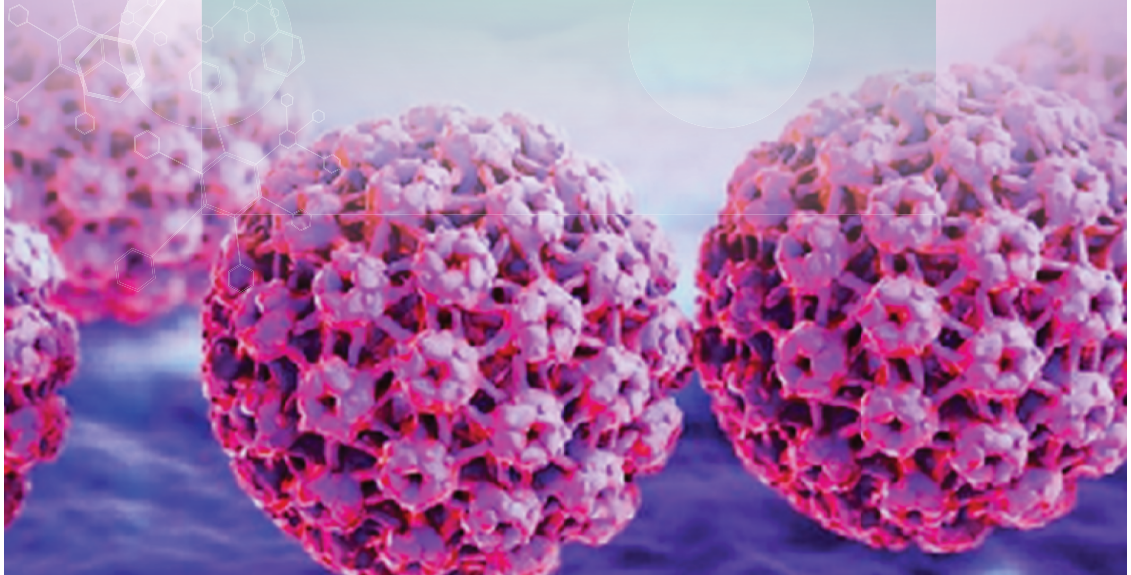
MINISTRY OF HEALTH MALAYSIA

GUIDELINES FOR PRIMARY HPV TESTING IN CERVICAL CANCER SCREENING IN MALAYSIA



FAMILY HEALTH DEVELOPMENT DIVISION
MINISTRY OF HEALTH MALAYSIA
2019

GUIDELINES FOR PRIMARY HPV TESTING IN CERVICAL CANCER SCREENING IN MALAYSIA

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FOREWORD

Cervical cancer is the 3rd commonest cancer among women and ranks the 7th amongst Malaysians. The incidence of cervical cancer has increased from 6.5 per 100000 population in 2011 year to 10.5 per 100000 population in 2018. The National Cancer Blue-Print 2016-2020 highlights the ministry's commitment towards control and prevention of cancer. Strategies to reduce the impact of cancer include early detection of cancers, creating awareness, training of healthcare providers, upgrading infrastructure and equipment for screening and multiagency collaboration.

Screening of cervical cancer was introduced in 1969, as a family services package, through the Maternal and Child Health Services. Conventional Pap Smear was the screening method used. Recent findings noted that nearly 95% of cervical cancer is caused by persistent infection by oncogenic strain of Human Papilloma Virus (HPV). Once infected with oncogenic strain HPV, it can take up to 10 years to convert healthy cervical cells into cancerous cells.

There are two (2) strategies in prevention of cervical cancer; that is providing HPV immunisation and early detection through effective screening. Malaysia has implemented the 1st strategy through the introduction of the HPV vaccination to 13-year old school girls in 2010. Implementation of HPV vaccination does not remove the need for cervical screening. However, the country has to implement a more effective screening method based on recent advances in screening and testing technology. As recommended by WHO, Malaysia will implement HPV DNA testing as a cervical screening modality. Besides it high sensitivity and specificity, this method is said to be able to eliminate barriers faced in the current cervical cancer screening Pap smear method.

This guideline is developed to assist health personnel in standardising the cervical cancer screening program as well as managing abnormal results of HPV Screening test.

I would like to congratulate and thank all the experts who have contributed towards the development of this revised guideline as well as those preceding it. I hope that this guideline will improve the programme performance and achieve the objective of reducing the incidence and mortality due cervical cancer among women in Malaysia.

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ABBREVIATIONS

AEC-US	Atypical Endocervical Cells of Undetermined Significant
ASC	Atypical Squamous Cells
CIN	Cervical Intra-Epithelial Neoplasia
GP	General Practitioner
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HSIL	High Grade Squamous Intra-Epithelial Lesion
IPES	Integrated Package of Essential Services
IPPF	International Planned Parenthood Federation
LBC	Liquid Based Cytology
LSIL/ LGSIL	Low Grade Squamous Intra-Epithelial Lesion
MOH	Ministry of Health
NAT	Nucleic Acid Test
PCR	Polymerase Chain Reaction
HSIL	High Grade Squamous Intra-Epithelial Lesion
SCC	Squamous Cell Carcinoma
SIL	Squamous Intra-Epithelial Lesion
STI	Sexual Transmitted Infection

1. INTRODUCTION

1.1 Cervical Cancer Screening in Malaysia

Cervical cancer screening in Malaysia using conventional Pap smear was initiated in 1969. It was initially introduced to all family planning acceptors. The importance of cervical cancer screening was further enhanced in 1995 when 'cancer' was chosen to be the theme of the Healthy Lifestyle Campaign. It became a national programme in 1995. The service later was expanded with the development of the "National Pap Smear Screening Programme" in 1998, to all eligible women age 20 – 65 years old yearly for the first 2 years and 3 yearly subsequently if the result are normal. Its' main objective were prevention and early detection of cervical cancer and ensuring early treatment as well as proper follow up of patients (Division of Family Health Development, 2004).

Every eligible woman is encouraged to come forward to have their Pap smear test done according to the schedule. The programme is carried out opportunistically, where women who attend the clinic for health screenings will be offered Pap smear screening.

The Ministry of Health provide sapproximately 75% of the Pap smear screening in the country without incurring any cost to the public. On the other hand, about 25% of the Pap smear screening service is provided by other agencies such as university hospitals, private facilities and non-government organisation but the women are required to payfor the tests. The main modality used for cervical cancer screening in the Ministry of Health facilities is conventional Pap smear, however, liquid-based cytology has been gradually introduced in 2014 to replace the conventional Pap smear. Liquid-based cytology (LBC) is a screening technique which isdeemed superior tothe conventional Pap smear (Strander, Andersson-Ellström, Milsom, Rådberg, & Ryd, 2007). In Malaysia, Liquid-based cytology has been initiated for cervical cancer screening in 2014 in several states namely Kelantan, Johor, Negeri Sembilan and Selangor (Division of Family Health Development, 2004).

1.2 HPV Vaccination Programme in Malaysia

With the announcement made by WHO in 2006, on the availability of effective, safe new HPV vaccines to prevent cervical cancer (United Nations Population Fund), the Ministry of Health, Malaysia (MOH) examined the possibilities of introducing HPV vaccination in Malaysia as a primary prevention strategy in addition to the existing cytology screening. The decision to proceed to this strategy was supported by local and international cost–effectiveness studies. Aljunid, et al (Ezat & Aljunid, 2010) who led a study on the local mathematical model of HPV vaccine, projected that the introduction of HPV vaccination will potentially prevent 89% of cervical cancer and save substantial annual cost for HPV-related treatment. Other considerations included vaccine efficacies (World Health Organization, 2017), high immunogenicity among adolescent, prophylaxis property of the vaccine and feasibility reasons.

Another strategy of prevention which is vaccinating girls before their sexual debut, and therefore before exposure to HPV infection, provides an excellent opportunity to decrease the incidence of cervical cancer over time. The National School-based HPV Immunisation Programme was launched in April 2010 targeting at the 13 yrs or Form 1 Malaysian female school children. This national programme was implemented in 2,958 public and private secondary schools registered under the Ministry of Education throughout Malaysia. The consent forms and printed HPV health education materials were delivered to the parents through school teachers one week prior to the first dose vaccination. This was done through scheduled school visits by the various school health teams at district level to ensure HPV vaccination spaced at the month 0, 1 and 6 must be completed within the same year. In 2017, in line with the SAGE (WHO) recommendation, the adolescent students were given only 2 doses of the HPV vaccine.

1.3 HPV and Cervical Cancer

In Malaysia, the incidence of cervical cancer (age-standardized rate) has increased to 10.5 per 100,000 population in 2018 (World Health Organization, 2018) compared to 6.5 per 100,000 population in 2011 (Azizah, Nor Saleha, Noor Hashimah, Asmah, & Mastulu, 2016). It is the third commonest cancer among women in Malaysia. The incidence increases at 35 years and peak between 50-74 years old.

Cervical cancer is a rare outcome of an unresolved HPV (oncogenic) infection, currently defined as persistent presence of HPV DNA in repeated testing of cervical specimens. Human papillomavirus (HPV) is the most common viral infection of the reproductive tract. Most sexually active women and men will be infected at some point in their lives and some may be repeatedly infected.

The peak time for acquiring infection for both women and men is shortly after becoming sexually active. HPV is sexually transmitted, but penetrative sex is not required for transmission. Skin-to-skin genital contact is a well-recognized mode of transmission.

Many of HPV types do not cause problems. HPV infections usually clear up without any intervention within a few months after acquisition, and about 90% clear within 2 years. There are about 40 genital HPV types, 14 are classified as oncogenic as they are associated with anogenital cancer, including squamous and adenocarcinoma of the cervix. HPV types 16 and 18 cause 70-80% of cervical cancer. However, while HPV is an extremely common genital infection, anogenital cancer is a rare outcome of its acquisition because most infections are cleared and progression from any persistent infection to invasive cervical cancer is generally slow. The immune system clears the virus within 1-2 years in the majority of those with genital HPV infection. Persistent infection with oncogenic HPV is associated with a significantly elevated risk of developing high grade cellular abnormalities of the cervix (Victorian Cytology Service Pathology (VCS), 2017).

In many industrialized countries, the prevalence of HPV infections in young adult females can range between 30% and 80%, and the lifetime probability of ever encountering HPV is as high as 80-90%. Most of these infections clear spontaneously without clinical signs or symptoms.

The fraction of persistent carriers of HPV into the middle ages is estimated to be at the range of 4-10% and these women are the true high-risk group for cervical cancer and probably for any other HPV-related cancer. In Malaysia, the reported incidence of HPV infection among healthy women is reported to be approximately 7%.

The time lag between the peak of HPV infection and the peak of cancer incidence is two (2) to four (4) decades, making the initial infections and precursor lesions of cervical cancer an appropriate target for screening and early detection. Despite significant gaps in knowledge, cervical cancer is the best understood of all cancers and model system for carcinogenesis.

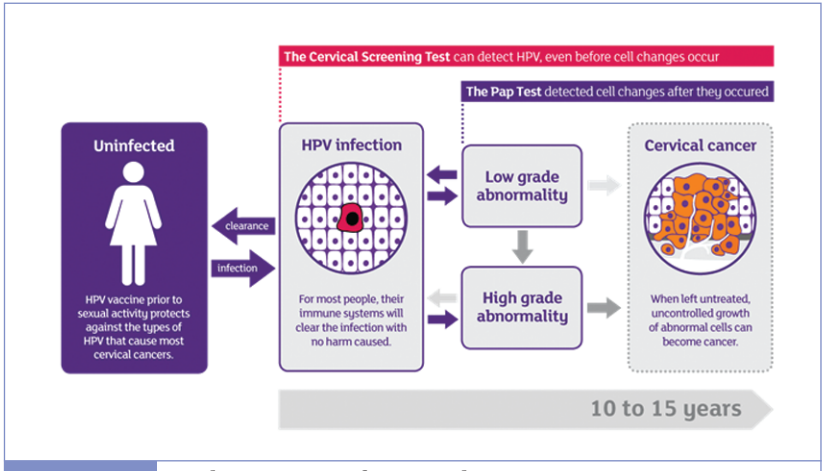


Figure 1 : Pathogenesis of cervical cancer

2. RATIONAL FOR PRIMARY HPV TESTING

The discovery of HPV as the necessary cause of cervical cancer has led to important technological advances, including the development of molecular tests for HPV to identify women with precancerous cervical lesions.

Cytological screening for cervical cancer precursors has been very successful in countries where adequate resources exist to ensure high quality and good coverage of the population at risk every three years. Mortality reductions in excess of 50% have been achieved in many developed countries; however the procedure is generally inefficient and unworkable in many parts of the world where the appropriate infrastructure is not possible.

Pap smear screening was initiated by the Ministry of Health (MOH) in 1969. Multi-agencies are involved in providing Pap smear screening services for Malaysian women in embracing the cancer screening programme. These agencies include MOH, the National Population and Family Development Board of the Ministry of Women, Family and Community Development, private clinics and hospitals, university hospitals and army hospitals. However, these screening programmesare opportunistic which caters those who come to the Maternal and Child Health Clinics.

In 1996, the second National Health & Morbidity Survey (NHMS II) revealed that only 26% of eligible women underwent cervical cancer screening using Pap smears while in 2006 (NHMS III) this proportion had doubled to 43.7%. However, five (5) years later, the NHMS 2011 reported that only 12.8% of eligible women had Pap smear examination (Institute for Public Health (IPH), 2008).

Substantial evidence exists to support the idea that HPV testing is advantageous both in triage of women with equivocal abnormal cytology, from surveillance after treatment of CIN lesions and in primary screening of women aged 30 years or older. However, the possible advantages offered by HPV-based screening require a well-organized programme with good compliance with screening and triage policies.

3. OBJECTIVE

- As a guide and reference for health personnel involved with cervical cancer screening.
- To standardize the cervical cancer screening programme in Malaysia.
- To standardize the management of abnormal result based on primary HPV screening test.
- To standardize management of the biopsy confirmed cervical pre invasive lesion.

4. SCREENING POLICY

4.1 Target age group

All sexually active women aged 30 to 49 years should be screened. Women less than 30 years (21-29) and 50-65 years are advised for Pap smear screening.

4.2 Screening intervals

The screening interval will be every 5 years for those who are tested HPV negative.

4.3 Management for HPV positive cases should follow the flow chart

4.4 Screening Personnel

Self-sampling by women or by health-care professional.

4.5 Reporting Personnel

Laboratory based: Scientific officer or pathologist.

Point-of-care test: trained healthcare professional in the health-care facility (as per approved by state POCT committee).

5. HOW TO TAKE A CERVICO-VAGINAL SAMPLE

5.1 Self-sampling (vaginal sample)

Instructions to women on self-sampling (English and Malay) (As per Figure 3 and 4).

HPV self-sampling kit can be in many forms as below:

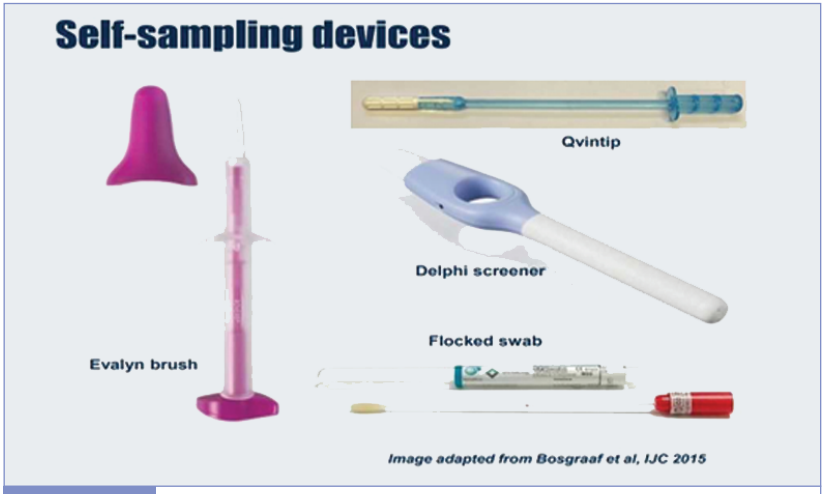


Figure 2 : Self-sampling devices

General guide for self-sampling technique (depend on the self-sampling devices available in the health facilities)

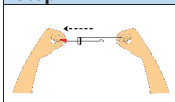
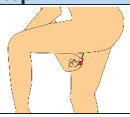
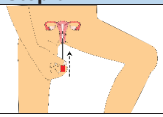
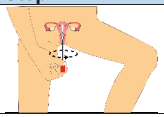
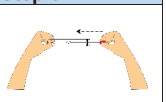
Step 1	Step 2	Step 3	Step 4	Step 5
				
SWAB • Remove the swab out of its plastic tube • Twist and pull	**POSITION** • Undress from the waist down • Remove your underwear • While holding the swab in your hand, get into a comfortable position	**INSERTING THE SWAB** • With your other hand, gently spread open the folds of skin at the opening of your birth canal • Insert the swab approximately 5cm (about half the length of your finger) • This is similar to inserting a tampon	**TAKING THE SAMPLE** • Rotate the swab gently for 10-30 seconds. There should be very little pain or discomfort • If you have any problems, speak to the nurse	**RETURN SWAB** • Put the swab back into the tube • Give the tube to the nurse

Figure 3 : Self-sampling HPV test English

Bagaimanakah cara untuk mengambil ujian HPV anda sendiri

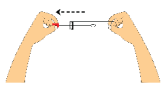
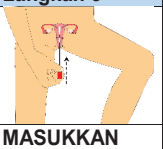
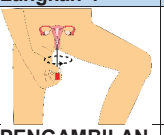
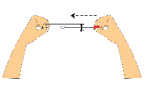
Langkah 1	Langkah 2	Langkah 3	Langkah 4	Langkah 5
				
KELUARKAN SWAB • Keluarkan swab dari tiub plastic • Pusing dan tarik • Guna pemegang tiub untuk meletakkan tiub swab	**KEDUDUKAN** • Tanggalkan pakaian dari aras pinggang ke bawah • Tanggalkan seluar dalam anda • Pastikan anda berada dalam kedudukan yang selesa	**MASUKKAN SWAB** • Gunakan tangan yang lain untuk membuka liputan kulit pada saluran faraj dengan perlahan • Pegang swab pada tanda merah • Masukkan swab mengikut aras yang ditetapkan	**PENGAMBILAN SAMPEL** • Putarkan swab sebanyak 10 kali. Anda mungkin mengalami kesakitan atau ketidakselesaan • Jika berhadapan sebarang masalah, sila rujuk kepada jururawat	**SIMPAN SWAB** • Masukkan semula swab ke dalam tiub • Serahkan tiub kepada jururawat

Figure 4 : Self-sampling HPV Test in Malay Language

5.2 By the health care provider-using self-sampling kit

Health-care professionals must be prepared to take the vaginal swabs for women who are not confident acquiring it. This can be taken with the patient in the supine position without a speculum.

5.3 Cervical smear using Liquid-base

Sample from cervical scrape is obtained using cervical brush/broom and suspended in a vial of preservative for transport to the laboratory. Refer Guidebook for cervical cancer screening.

6. REQUIREMENT FOR HPV SAMPLING IN HEALTH CLINICS

6.1 Self-sampling

- Request forms. (Based on BORANG PERMOHONAN UJIAN HPV/PAP SMEAR (PS 1/98 (Pindaan 2019)).
- Flocked swab (Not to be replaced by other swab for example cotton or microbiology swab) or any types of sampling device
- Specimen container with preservative.
- Laminated guide for women

6.2 Cervical smear using LBC (follow Guidebook for cervical cancer screening)

7. HOW TO PREPARE THE SAMPLE BEFORE SENDING TO LABORATORY

7.1 The detail of the preparation will be explained by the manufacturer.

7.1.1 Self-sampling

- Label the samples and request forms with 2 unique identifiers (preferably using barcode).

- Suspend the flocked swab into the container with preservative fluid/any other sampling device which will follow the preparation manual from the manufacturer.
- Tighten the cap to prevent spillage or contamination.
- Place the samples into biohazard plastic bag.
- Send the samples at room temperature (**stable up to 35^{0}C**) with the request forms to the designated laboratory.

7.1.2 **LBC sampling (follow Guidebook for cervical cancer screening)**

8. HPV TESTING

8.1 The platform

HPV DNA testing has been shown to be more effective than cervical cytology in detection of precancerous changes of the cervix. HPV can be detected through tests that identify high-risk HPV types, either by signal amplification (hybridization techniques) or target amplification (PCR) of a viral DNA fragment (with partial genotyping).

In the clinical setting where self-sampling is utilized, PCR based target amplification has consistently been shown to have higher sensitivity and greater clinical utility and therefore only PCR based tests can be used to test self-collected samples. Furthermore, in the context of self-collection, the platform should offer a cellularity control, to avoid “false negative” results due to the swab not being inserted into the vagina.

Laboratory based HPV test must be clinically validated in population studies (FDA approved or CE-IVD (European Conformity, in vitro diagnostic for specimens derived from humans) marked, both MDA approved). Alternatively, tests that are

FDA approved or CE-IVD marked, (both MDA approved) and have been validated in cross sectional comparisons with other validated tests, using the benchmarks articulated by Meijer et al. (Meijer, Berkhof, Heideman, Hesselink, & Snijders, 2009) may be used.

In order to ensure compliance to a Good Laboratory Practice, each designated laboratory shall have a test protocol in place.

8.2 The location

HPV testing can either be performed in a central laboratory (batch testing) or as Point of care test (POCT) (as per approved by state POCT committee), depending on geographical area and resource accessibility. Furthermore, for laboratory-based HPV test, the test selected must be clinically validated in population studies (FDA approved or CE-IVD marked, both MDA approved) and performed in accredited laboratories (under Molecular Lab/Unit). On the other hand, several validated POCT ports will be placed in selected healthcare facilities and managed by an authorized personnel.

8.3 Technology/principle:

Clinically validated HPV test (minimum FDA/CE certified or equivalent) and MDA certified (under Act 737) is to be utilised in this screening.

Table 1: Some Examples of Available HPV Nucleic Acid Test (NAT) Methodology

TEST	TECHNIQUE	NAME
DNA	Target Amplification	GP5+/GP6+ bio PCR-EIA
	Amplification and genotyping of HPV-16 and HPV-18	Cobas HPV test (Roche) Xpert HPV (Cepheid) Abbott Real Time High Risk (HR) HPV assay PapilloCheck Onclarity (BD) Anyplex II (Seegene)
RNA	Amplification of E6/E7 proteins	Aptima HPV Assay PreTect HPV-Proofer HV

The clinical sensitivity of a HPV test is an important consideration for the use of the test in screening programmes. POCT sensitivity is more than 90% while the specificity is more than 40%. For a laboratory-based HPV testing, its sensitivity is 90% and the specificity is more than 80%.

8.4 Current available platforms

The current available molecular platforms in most state hospitals which are used for infectious diseases screening can be used for HPV testing. With this transformation program, the workload of HPV testing will increase and will require additional equipment. This can be done by reagent rental or placement. Therefore, the test can also be outsourced to the accredited private institutions/ laboratories.

8.5 Specimen Collection (will be explained by the manufacturer)

The medium/device used by practitioners or clients (self-sampling) to collect the lower vaginal specimen must be suitable and validated for use with HPV test as intended by the manufacturer.

The specimen container must be screwed on properly to prevent spillage or contamination. The specimen shall be properly labelled and accompanied with relevant clinical history using 'BORANG PERMOHONAN UJIAN HPV/PAP SMEAR (PS 1/98 (Pindaan 2019)).

8.6 Transportation of specimen (will be explained by the manufacturer)

Specimen should be transported as soon as possible. (should not exceed 14 days after collection). It does not require cold-chain management but should be stored at room temperature (<30°C).

9. ANALYTICAL PROCESS

- The test shall be performed by authorized and competent personnel.
- The test procedure shall follow the manufacturer's insert kit.
- The laboratory must demonstrate the validation of the collection device by referring to peer reviewed publication or by undertaking its own validation studies.
- The 'Lab Turn-Around Time' LTAT should be within 5 working days.

10. RESULT

- The result is reported qualitatively:
  - Positive for HPV 16/18
  - Negative for HPV 16/18
  - HPV non-16/18 subtype
  - Unsatisfactory.
- Result is unsatisfactory if the Internal Control is invalid.
- An example of the report is portrayed in Table 2.
- The result shall be conveyed to the requesting officer via web-based, email, fax or hard-copy.
- Leftover specimen shall be kept at room temperature for at least 2 weeks after the report has been released and can be stored up to 4-10 weeks if kept at 2-8°C.

Table 2: Example of a HPV Test Report

SPECIMEN	Cervico-vagina
TEST RESULTS	PCR for Oncogenic HPV and genotype: HPV 16 – Detected/Not Detected HPV 18 – Detected/Not Detected HPV (non-16/18) – Detected/Not Detected INVALID
RECOMMENDATION	**Follow the 'Management of HPV Result'**

11. WASTE DISPOSAL

Disposal of leftover specimens shall follow the standard guideline of clinical waste management.

12. REFLEX LIQUID BASED CYTOLOGY (LBC)

Liquid Based Cytology is indicated in cases of positive HPV non-16/18. The specimen collection shall be carried out by the clinician.

The collected specimen shall be sent to designated cytology laboratory which is equipped with adequate resources for example equipment, dedicated, trained cytotechnologists and anatomical pathologists. The laboratory shall participate in Quality Assurance Programme and comply with International Standard of Medical Laboratory Accreditation (ISO 15189). The reporting format shall follow the PS 2/2019 format.

13. MANAGEMENT OF HPV RESULTS(COMMUNICATION OF RESULTS AND AUDIT)

Please refer to Figure 5 below for the summary of clinical management.

- Unsatisfactory: For women with an unsatisfactory HPV test, offer a repeat test within 12 weeks.
- Negative high risk HPV: For women with a negative HPV test, they should be offered the next screening test not earlier than 5 years.
- High risk positive 16/18: Women with a positive oncogenic HPV (16/18) test result should be referred directly for colposcopic assessment
- High risk positive non-16/18: Women with a positive oncogenic HPV (not 16/18) test result, liquid based cytology should be performed. Those with a negative/ASC-US or LSIL LBC should have a repeat HPV test in one year. For those with ASC-HorHSIL, referral for colposcopy should be made. In the case where a LBC report suspicious for SCC or any glandular abnormality, referral to a gynaecological oncologist.

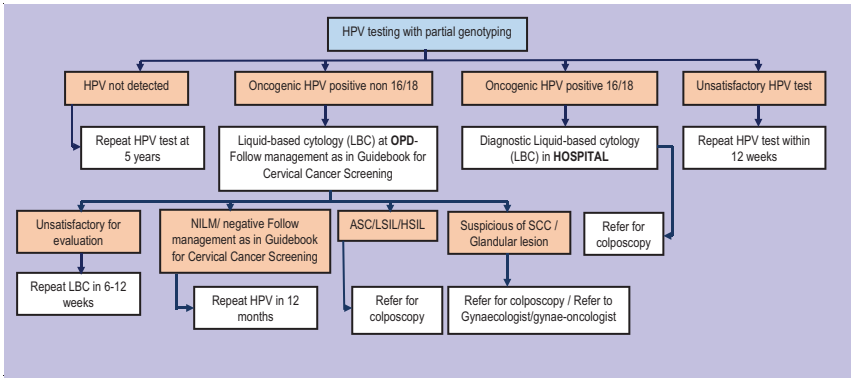


Figure 5 : Management of HPV results

14. DIAGNOSIS AND TREATMENT

Patients with positive HPV results require further diagnosis and treatment. They should be referred to hospitals with facilities (hospitals with specialists) for colposcopic assessment. However, in very remote areas, specialists or trained medical officers can perform visual assessment for treatment (local ablative therapy-cryotherapy or thermocoagulation.

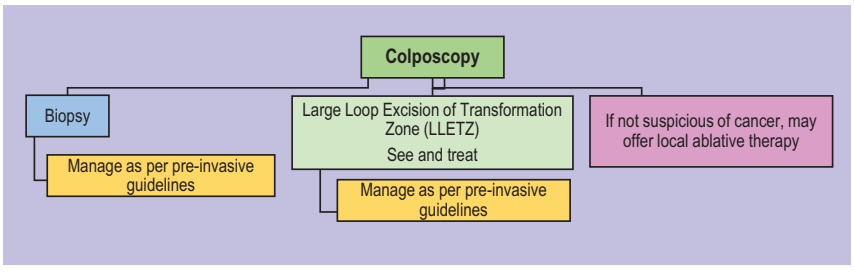


Figure 6 : General approach for diagnosis and treatment

15. COUNSELLING AND OPTIONS FOR MANAGEMENT

15.1 Colposcopy

The options available to women who attend colposcopy will depend on the patient preference, clinical judgement and facilities available at the hospital. For patients who are most likely to default and not come for subsequent visits, a 'see and treat' option is recommended. If the colposcopic service is not available, local ablative therapy can be offered when invasive cancer is clinically ruled out.

15.2 Local ablative therapy

The modes of local ablative therapy is determined by expertise and availability of cryotherapy (cold-coagulation). Can be performed by a minimum level trained medical officer. However, the medical officer should be by a senior specialist.

15.3 Follow-up

For patients who have received treatment of pre-invasive disease or ablative therapy, they should be followed up in 12 months with HPV DNA testing. HPV testing can be done at primary care setting.

16. TRAINING OF HEALTHCARE WORKERS

16.1 The healthcare workers will require training prior to starting the HPV screening programme. This involves all levels of personnel at primary care level, family medicine specialists, nurses, gynaecologist, pathologists, medical officers, assistant medical officers, scientific officers and medical laboratory technologists.

16.2 Training objectives:

These objectives are to enable the health care professionals to:

- Communicate information about HPV testing and cervical cancer screening.
- Teach and assist lower vaginal sampling for HPV testing.
- Provide information and counselling to women, before and after the HPV test is taken.
- Communicate and convey the HPV result in the most appropriate manner.
- Ensure proper follow-up according to the available guidelines.

16.3 Training topics (please refer to the training modules)

- Anatomy of the female reproductive system.
- HPV infection and cervical cancer.
- Taking a sample and preparing for Liquid Based Cytology on cervical lesion.
- User training for HPV DNA tests.
- Cytology interpretation of cervical lesion.

17. EDUCATION MATERIAL

Please refer to the education materials that have been prepared

18. EQUIPMENT

18.1 Hospital equipment required for basic colposcopy service:

- Colposcopy couch
- Colposcope (+/- camera system)
- Doctor's chair
- Insulated speculum
- Smoke extractor

- Diathermy machine for LLETZ
- Dental syringe
- Acetic Acid +/- Lugol's iodine
- Monsel's solution
- Basic dressing set
- Biopsy forceps

18.2 Laboratory requirements

The equipment and consumables for HPV testing and reflex Liquid-based Cytologyshall be acquired through tender process either by state, regional or centrally based on COST PER TEST for proposals that meet the technical requirements articulated in section 8 above.

19. QUALITY ASSURANCE FOR BATCH TESTS

19.1 Laboratory

The laboratory should comply with ISO 15189 standard and have a documented quality assurance process that includes (but is not limited to) the following:

19.1.1. Sampling

Internal Quality Control (QC) shall be included to assess the adequacy of the human DNA material present in the sample. The laboratory should monitor the rate of unsatisfactory specimens and provide feedback to referring clinicians.

19.1.2. Analytical

- Positive and Negative Control shall be included in every batch of test.
- The laboratory shall participate in External Quality Assurance (EQA) Programme for HPV test and Gynae-cytology.

20. INFORMATION SYSTEM AND MONITORING

20.1 Short term monitoring

Data are entered manually into the excel sheet provided to each clinic. Each clinic is required to identify an officer to monitor the implementation of the services. In order to smoother the communication between the primary care and the hospitals, the hospital laboratories atthe designated hospitals and gynaecology clinicsare also required to identify officersto liaise with the liaison officers at the health clinics.

20.2 Plan for the future

A networking system is hoped to be developed between the primary and secondary/tertiary care in order to enable sharing of data.

21. FLOWCHART FOR HPV DNA TESTING

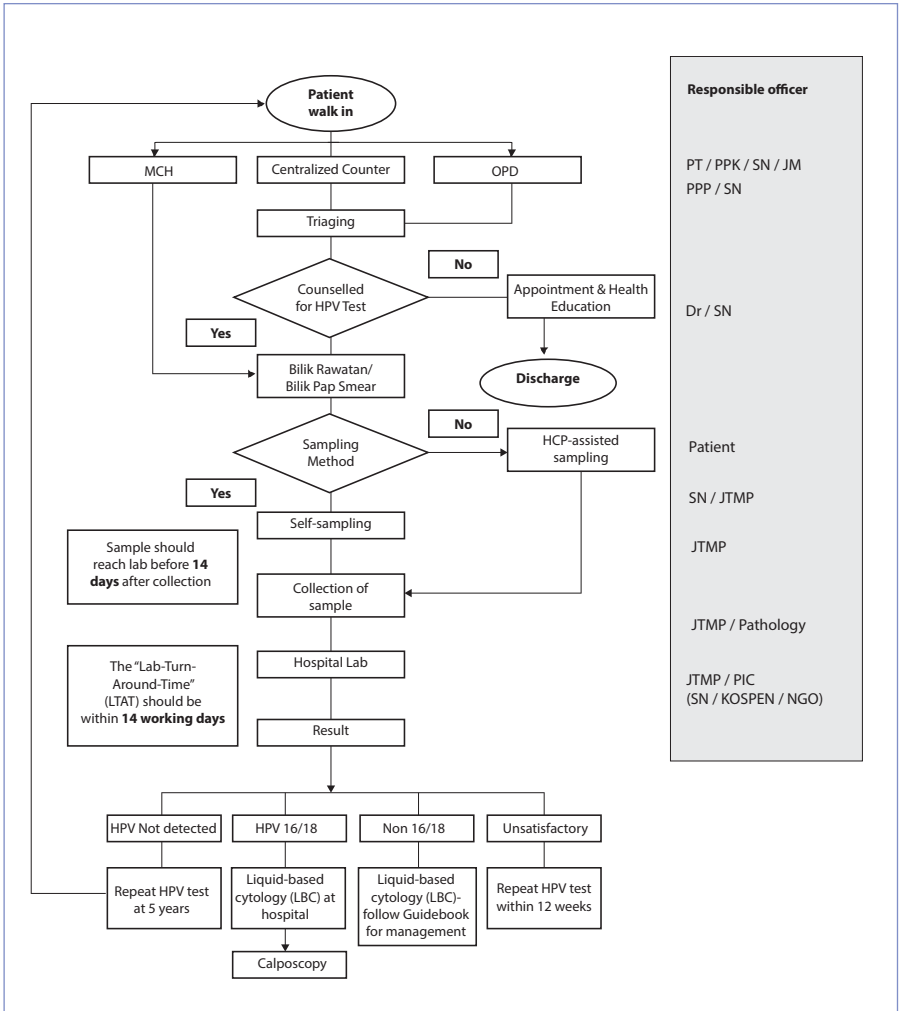


Figure 7 : Flowchart for HPV Testing

APPENDIX 1

PS 1/98 (Pindaan 2019)

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI

No. Makmal:

BORANG PERMOHONAN UJIAN HPV/ SITOLOGI (PAP SMEAR /LBC)
HPV TEST /CYTOLOGY (PAP SMEAR/LBC) REQUEST FORM

Hospital / Klinik
Hospital / Clinic

BUTIRAN PELANGGAN / *CLIENT'S BIODATA*

i. Nama / *Name* :

ii. No Kad Pengenalan / *IC. No*

iii. Etnik / *Ethnicity* :

iv. Umur / *Age* :

v. Alamat : *Address*

vi. No Telefon: *Phone No* (Rumah/ *Home*) (Pejabat/ *Office*)

BUTIRAN SARINGAN / *SCREENING INFORMATION (Tandakan X pada kotak bekenaan)*

i. Tarikh sampel diambil: *Date sample taken*

ii. Jenis Sampel: *Type of sample*
- ☐ Conventional Pap Smear
- ☐ Liquid-based preparation
- ☐ Cervical vagina swab for HPV

iii. Bahagian sampel diambil: *Sample site*
- ☐ Serviks / *cervix*
- ☐ Vagina / *Vagina*

iv. Jenis saringan: *Type of screening*
- ☐ Pertama / *new*
- ☐ Ulangan / *repeat*

v. No. Makmal terdahulu: *Previous Laboratory No.*
- *HPV*
- *Pap Smear*
- *Histopathology*

vi. Keputusan terdahulu: *Previous diagnosis*

vii. Pengambilan Sampel Oleh *Sampling by* ☐ Sendiri ☐ Warga Kesihatan

RINGKASAN KLINIKAL / *CLINICAL SUMMARY (Tandakan X pada kotak bekenaan)*

i. Status Hormon: *Hormonal status*
- ☐ Hamil / *Pregnant*
- ☐ Postpartum / *Postpartum*
- ☐ Pra-menopos / *Pre menopausal*
- ☐ Pos-menopos / *Menopausal*

ii. Tarikh Haid terakhir: *Last menstrual period*

iii. Tarikh Kelahiran terakhir: *Last childbirth*

iv. Kontraseptif /Terapi hormon: *Contraceptive/ hormonal therapy:*
- ☐ ADR / *IUCD*
- ☐ Hormon / *Hormone*
  Nyatakan / *Specify*:.....
- ☐ Tiada / *None*

v. Sejarah Rawatan : *Treatment history*
- ☐ Kemoterapi / *Chemotherapy*
- ☐ Radiasi dibahagian pelvik / *Pelvic radiation*
  Nyatakan tarikh akhir rawatan:
  Specify completion date:.....
- ☐ Pembedahan ginekologi / *Gynaecology surgery*
  Nyatakan / *specify*:.....
  .....
- ☐ Tiada / *none*

vi. Gejala / Tanda: *Symptom / Sign*
- ☐ Tiada / *Nil*
- ☐ Lelehan dari faraj / *Vaginal discharge*
- ☐ Pendarahan luar biasa / *Abnormal bleeding*

  Nyatakan / *specify* :.....
  .....

vii. Serviks : *Cervix*
- ☐ Biasa / *Normal*
- ☐ Luar Biasa / *Abnormal*
- ☐ Tiada serviks / *Absent cervix*

viii. Maklumat tambahan: *Additional information* .....
.....
.....

- Tahun Akhir Saringan Pap smear / HPV Diambil

MAKLUMAT PEMOHON / *REQUESTING PRACTITIONER*

Nama : *Name*

Jawatan / COP: *Designation / Stamp*

Tanda Tangan : *Signature*

APPENDIX 2

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI
FORMAT LAPORAN SITOLOGI (PAP SMEAR/LBC)
PAP SMEAR/ LIQUID BASED CYTOLOGY(LBC) REPORT

PS 2/ 2019

Name: **IC No:** **Cytology No:**

A) Type of sample: ☐ Conventional Pap Smear ☐ Liquid-based preparation

Ai) Type of LBC: ☐ SurePath ☐ ThinPrep ☐ Others

B) Sample Adequacy:

☐ **i) Satisfactory for evaluation :**

Endocervical cells / transformation zone cells:
☐ Present ☐ Absent
With:
☐ Obscuring blood
☐ Poor fixation / air drying artifact
☐ Thick uneven smear
☐ Thick inflammatory exudate
☐ Lack of clinical data

☐ **ii) Unsatisfactory for evaluation:**
☐ Scanty squamous epithelial component
☐ Poor fixation / air drying artifact
☐ Obscuring blood
☐ Thick uneven smear
☐ Thick inflammatory exudate
☐ Broken slide beyond repair

C) Interpretation / Result

☐ **i) Negative for intraepithelial lesion or malignancy (NILM)**

a) Organism present :
☐ Fungal organisms morphologically consistent with Candida spp.
☐ Shift in flora suggestive of bacterial vaginosis
☐ Bacteria morphologically consistent with Actinomyces spp.
☐ Cellular changes associated with Herpes Simplex Virus
☐ Trichomonas vaginalis
☐ Cytomegalovirus (CMV)

b) Other non-neoplastic findings:
☐ Benign cellular changes associated with:
☐ inflammation / typical repair
☐ irradiation
☐ Intrauterine contraceptive device (IUCD)
☐ Atrophy
☐ Presence of glandular cells post hysterectomy
☐ Presence of endometrial cells (in woman ≥45 yrs of age)

☐ **ii) Epithelial cells abnormalities**

☐ **a) Squamous cell:**
☐ Atypical squamous cells:
☐ of undetermined significance (ASC-US)
☐ cannot exclude HSIL (ASC-H)
☐ Low grade squamous intraepithelial lesion (LSIL)
☐ High grade squamous intraepithelial lesion (HSIL):
☐ Features suspicious for invasion
☐ Squamous cell carcinoma

b) Glandular cells:
☐ Atypical cells (NOS):
☐ Endocervical cells
☐ Endometrial cells
☐ Glandular cells
☐ Atypical cells , favour neoplastic:
☐ Endocervical cell
☐ Glandular cells (NOS)
☐ Endocervical adenocarcinoma (in-situ)
☐ Adenocarcinoma:
☐ Endocervical
☐ Endometrial
☐ Extrauterine
☐ Not otherwise specified (NOS)

c) Other malignant neoplasm, specify:
.....
.....
.....

D) Comments : .....
.....
.....

E) Suggestion
☐ Repeat LBC/ Pap Smear as Schedule
☐ Repeat Pap Smear 3-6 month
☐ Repeat Pap Smear after antimicrobial treatment
☐ Repeat smear after oestrogen therapy
☐ Refer FMS
☐ To get Colposcopy appointment
☐ Refer to Gynaecologist / Gynaecological Oncologist

LAB USE ONLY

Validated by		**Screener**	
Designation		First Screener	
Date reporting		Second Screener	
Date Printing		Pathologist	

Review of previous Pap smear slide :
YES / NO (If YES Slide No: ☐)

VALIDATION

Result reviewed by:	Date :
Designation / Stamp:	Action :

APPENDIX 3

KEMENTERIAN KESIHATAN MALAYSIA
PERKHIDMATAN PATOLOGI
BORANG PERMOHONAN UJIAN HPV/SITOLOGI (PAP SMEAR/LBC)

HPV 2/2019

MOLECULAR VIROLOGY TEST RESULT REPORT

Human Papillomavirus (HPV) Genotyping

NAME :
NRIC NO. :
REGISTRATION NO. :
WARD / KLINIK :
HOSPITAL :
NEGERI :
REQUESTED BY :

SAMPLE DETAILS FOR MOLECULAR VIROLOGY TEST

Sample Type	☐ Self sample ☐ LBC	Date of Test	-
Sample Collection Media		Lab Barcode No.	-
		Date of Sample Collection	-
Sample Transport Condition	☐ with ICE ☐ no ICE	Date of Sample Received	-

RESULT DETAILS FOR MOLECULAR VIROLOGY TEST

QUALITITATIVE Real-time PCR - HPV VIRUS DNA			
Result Interpretation (Tanda X pada kotak berkenaan)	HPV 16	Detected	
		Not Detected	
	HPV 18	Detected	
		Not Detected	
	HPV (non 16/18)	Detected	
		Not Detected	
		INVALID / UNSATISFACTORY	

NOTES :

a) Test method : Real-Time Polymerase chain reaction (RT-PCR).
b) Genotype detection : 16, 18 and other High Risk HPV DNA (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)
c) 'Not Detected' result does not conclusively rule out the agent tested, for the following reasons:
- *Specimens collection not timely.*
- *Specimen deterioration / breakdown of cold chain during storage or transportation.*
- *Detection value lower than limit of detection.*

d) This result shall be interpreted in conjunction with other clinical laboratory findings.
e) This report shall not be reproduced except with written approval from the laboratory.

COMMENTS :

SUGGESTION

☐	Repeat HPV test at 5 years (HPV not detected)
☐	Repeat HPV test within 12 months (Unsatisfactory HPV test)
☐	For Liquid Based cyctology (LCB) (HPV Positive non 16/18)
☐	Refer for COLPOSCOPY (HPV Positive 16/18)

Authorized by:

..... Date : .....

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