

# ANNEX 6. ADDITIONAL INFORMATION FOR SCREENING AND TREATMENT RECOMMENDATIONS

**Quality assurance:** A quality-assured programme is one that is monitored to give assurance that the results consistently achieve the highest level of accuracy and reliability for the detection and treatment of cervical abnormalities by the modality chosen.

**Other programme information:** Screening registries, and call-and-recall efforts to ensure that women are managed appropriately are essential for both organized and opportunistic programmes. Strong links need to be established between individual patients and the multiple levels of health services (primary care level, hospital level) to ensure the continuity and completion of care.

**Self-collected samples:** When a patient obtains the swab from their vagina for the screening test (high-risk human papillomavirus, HPV, DNA test). The majority of current laboratory-based HPV screening tests rely on cervical specimen collection by a clinician. However, self-collected samples for HPV testing provide an additional strategy to overcome cultural and logistical barriers towards accessing the health system and the reference laboratory or hospital screening programme.

There are many products for the self-collection of cervical specimens designed as kits with a single-use swab or cervical brush and a tube containing the collection/transport medium.

The self-collection process follows similar steps for most products: (i) insert the swab/brush into the vagina and gently rotate for 10–30 seconds; (ii) remove the swab/brush and transfer it into the collection tube; (iii) snap off the swab/brush shaft and cap the collection tube; (iv) discard the shaft; and (v) label the collection tube and send the sample to a laboratory. Specimens are stable at room temperature for at least 24 hours (and for some kits, for more than 30 days). For the most part, the self-collection process is acceptable to women and perceived as discreet, private and time-saving. The process is described by participants as female-friendly, painless and quick.<sup>4</sup>

**HPV tests:** The nucleic acid amplification testing (NAAT) technologies have led to the development of HPV in vitro diagnostic medical devices for screening that focus on the qualitative detection of the high-risk genotypes of HPV. Several in vitro diagnostic medical devices for HPV NAAT have been developed to specifically detect the most common oncogenic genotypes, HPV types 16/18, and in turn to identify those women at the highest risk of developing cervical cancer. Molecular HPV testing is based on the detection of HPV DNA from high-risk HPV types in vaginal and/or cervical

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<sup>4</sup> Screening and treatment of pre-cancerous lesions for secondary prevention of cervical cancer: technology landscape. Geneva: World Health Organization; 2019; p. 12 ([https://unitaid.org/assets/Cervical\\_Cancer\\_Technology-landscape-2019.pdf](https://unitaid.org/assets/Cervical_Cancer_Technology-landscape-2019.pdf), accessed 9 April 2021).

samples, and most laboratory tests can detect up to 15 HPV types. HPV tests can either detect the high-risk HPV genotypes in bulk without distinguishing the individual types or can detect separate HPV types via genotyping capacity. See *WHO technical guidance and specifications of medical devices for screening and treatment of precancerous lesions in the prevention of cervical cancer*.<sup>5</sup>

There are a large number of HPV tests available in different formats, and new ones continue to become available; clinicians and public health decision-makers should be very careful when selecting one technique from the broad variety available in the market, using analysis on the basis of documented information about the clinical validation for the required purpose.

See *Introducing and scaling up testing for human papillomavirus as part of a comprehensive programme for prevention and control of cervical cancer: a step-by-step guide*.<sup>6</sup>

The effect of the HPV vaccination effort to reduce the prevalence of HPV will affect the characteristic positive and negative predictive values of HPV tests. Recommendations will soon be re-evaluated to take this into consideration as more women who have been previously vaccinated move into the age ranges for cervical cancer screening.

**Visual inspection with acetic acid (VIA):** VIA is a direct visual assessment of the cervix using a 3–5% acetic acid solution to visibly whiten cervical lesions, which temporarily produces what is known as an acetowhite lesion. This appears after 1 minute and may last 3–5 minutes in the case of CIN2/3 and invasive cancer. VIA is appropriate to use in women whose transformation zone is visible (typically in those younger than 50 years). This is because once menopause occurs, the transformation zone, where most pre-cancer lesions occur, frequently recedes into the endocervical canal and prevents it from being fully visible.

It is difficult to establish and maintain quality assurance with VIA programmes. This can make the sensitivity and specificity of VIA testing quite variable. See *WHO technical guidance and specifications of medical devices for screening and treatment of precancerous lesions in the prevention of cervical cancer*.<sup>7</sup>

**Cytology:** The Papanicolaou (Pap smear) or liquid-based smear test checks whether cells in the cervix are abnormal. Cells are collected via speculum examination with a brush and swab, and placed either directly onto a slide to which a fixative is added (conventional cytology) or placed in a bottle with a liquid storage media (liquid-based cytology). Abnormal cervical cells testing as “atypical squamous cells of uncertain significance (ASCUS), low grade to high grade” may mean that there are pre-cancer changes in the cervix that may lead to cervical cancer.

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<sup>5</sup> WHO technical guidance and specifications of medical devices for screening and treatment of precancerous lesions in the prevention of cervical cancer. Chapter 2 and Annexes 2A and 2B. Geneva: World Health Organization; 2020 (<https://apps.who.int/iris/bitstream/handle/10665/331698/9789240002630-eng.pdf>).

<sup>6</sup> Introducing and scaling up testing for human papillomavirus as part of a comprehensive programme for prevention and control of cervical cancer: a step-by-step guide. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/item/9789240015166>).

<sup>7</sup> WHO technical guidance and specifications of medical devices for screening and treatment of precancerous lesions in the prevention of cervical cancer. Chapter 4 and Annex 3. Geneva: World Health Organization; 2020 (<https://apps.who.int/iris/bitstream/handle/10665/331698/9789240002630-eng.pdf>).

In this guideline, ASCUS in the presence of high-risk HPV DNA was used as the cut-off for an abnormal test that would need further evaluation. If a cytology test is positive, a woman may need to have the cervix examined or may need a further test (such as an HPV DNA test), or could receive ablative or excisional treatment to have the pre-cancer lesion removed.<sup>8</sup>

**Colposcopy:** A colposcope is a low-magnification, light-illuminated visualization instrument primarily used alongside screening tools for screening, diagnosing and managing cervical pre-cancer lesions. It allows the examiner to view the epithelial tissues of the cervix and anogenital areas. For the purposes of cervical pre-cancer assessment, it helps to determine the transformation zone type and the grade of suspected epithelial abnormality. In addition, colposcopy facilitates and optimizes biopsy and excisional treatment. Training and supervision are needed to acquire colposcopy proficiency.

Traditionally, a colposcope is a free-standing machine held on a stand or legs, with magnification. Newer types of colposcopes are portable, and some can even attach to a typical mobile phone. This has made colposcopy much more accessible to all resource settings. See *WHO technical guidance and specifications of medical devices for screening and treatment of precancerous lesions in the prevention of cervical cancer*.<sup>9</sup>

**Histology:** The diagnosis of CIN is established by a histopathological examination of tissue such as obtained through cervical punch biopsy or endocervical curettage or excision. The accuracy of the histological diagnosis of CIN is dependent on the quality of the sample, the site of the biopsy, its preparation in the laboratory and its interpretation.<sup>10</sup>

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<sup>8</sup> Koliopoulos G, Nyaga VN, Santesso N, Bryant A, Martin-Hirsch PPL, Mustafa RA, et al. Cytology versus HPV testing for cervical cancer screening in the general population. *Cochrane Database Syst Rev*. 2017;8:CD008587.

<sup>9</sup> WHO technical guidance and specifications of medical devices for screening and treatment of precancerous lesions in the prevention of cervical cancer. Chapter 4. Geneva: World Health Organization; 2020 (<https://apps.who.int/iris/bitstream/handle/10665/331698/9789240002630-eng.pdf>).

<sup>10</sup> Castle PE, Schiffman M, Wheeler CM, Wentzensen N, Gravitt PE. Impact of improved classification on the association of human papillomavirus with cervical precancer. *Am J Epidemiol*. 2010;171(2):155–63. doi:10.1093/aje/kwp390.