

Private Sector Dialogue on Cervical Cancer Elimination

Strengthening concerted action to achieve the 2030 targets for cervical cancer elimination

Discussion Paper¹: Expanding access to products and services for secondary prevention– Human papillomavirus (HPV) Nucleic Acid Technique (NAT) Assays

1. Introduction

Cervical cancer is preventable and curable if it is detected early and managed effectively. However, it is the 4th most common form of cancer among women worldwide, with approximately 660,000 women diagnosed in 2022. In addition, cervical cancer claimed the lives of almost 350,000 women in 2022 with over 90% of those deaths occurring in low- and middle-income countries.^{2,3}

In May 2018, the WHO Director-General announced a global call for action to eliminate cervical cancer, underscoring renewed political will to make elimination a reality and calling for all stakeholders to unite behind this common goal. In 2020, 194 Member States adopted the *Global strategy to accelerate the elimination of cervical cancer as a public health problem* (herein referred to as the Global Strategy). Within this resolution WHA73.2, the Director-General was provided a mandate to “to support the implementation of the global strategy to accelerate the elimination of cervical cancer as a public health problem, including through domestic support to Member States in implementing the global strategy, with assistance to improve the availability, affordability, accessibility, utilization and quality of associated products; to prioritize support for high-burden countries to bring evidence-based interventions to scale; and to collaborate with stakeholders to strengthen engagement, coordination, research, innovation, and resource mobilization.

The Global Strategy outlines the path to the elimination of cervical cancer. First, all countries are encouraged to reach and maintain an incidence rate of below 4 per 100,000 women. Achieving that goal rests on three key pillars (vaccination, screening, treatment) and their corresponding targets to be achieved by 2030 to get on the path to elimination within the next century:

- 90% of girls fully vaccinated with the HPV vaccine by the age of 15
- 70% of women screened using a high-performance test by the age of 35, and again by the age of 45
- 90% of women with pre-cancer treated and 90% of women with invasive cancer managed

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² Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, *et al.* Global Cancer Observatory: Cancer Today (version 1.1). 2024. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.who.int/today>, accessed 11 June 2024.

³ Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018 Nov;68(6):394-424.

2. Approach to the Private Sector Dialogue on Cervical Cancer Elimination

Following the September 2011 United Nations (UN) High-Level Meeting on the Prevention and Control of Non-Communicable Diseases (NCDs), WHO has led a series of consultations with Member States, UN agencies, Nongovernmental Organizations (NGOs), academic institutions, philanthropic foundations, and the private sector to promote and monitor global action in realizing the commitments made in the UN Political Declarations on the Prevention and Control of NCDs in 2011, 2014 and 2018.

Pursuant to World Health Assembly resolution WHA73.2, the WHO Secretariat, through the Department of Noncommunicable Diseases, in collaboration with the Division of Access of Medicines and Health Products, is convening a series of biannual dialogues with the private sector. These are organized in accordance with relevant WHO policies, including the framework of engagement with non-State actors. The private sector dialogues aim to define meaningful and effective contributions to the implementation of national responses for the prevention, management, and control of NCDs and the attainment of related Sustainable Development Goals (SDGs) 3.4, 3.8, and 3b by improving access to, and affordability of safe, effective, and quality-assured medicines and health technology products; reducing by one-third premature mortality from NCDs through prevention and treatment; and promoting mental health and wellbeing.

The upcoming dialogue, will focus on Cervical Cancer Elimination and HPV testing for cervical cancer screening. In preparation, WHO has developed this discussion paper in a concerted effort to collectively strengthen and achieve the 2030 targets for cervical cancer elimination through increased access to HPV testing.

Effective interventions will require enhanced collaboration and commitment for greater impact at the country level. In response, WHO will provide leadership and coordination in promoting and monitoring global action to fulfill the commitments made in these resolutions and will use the approach outlined below:

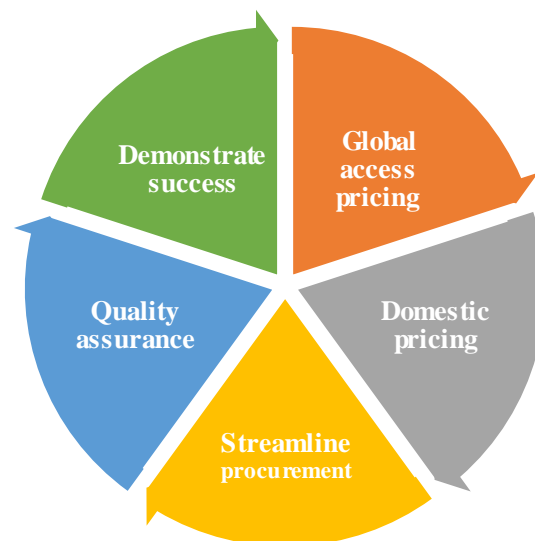
1. Engage with the private sector, taking into account national health priorities and objectives for its meaningful and effective contribution to the implementation of national responses to NCDs in order to reach Sustainable Development Goal Target 3.4, 3.8, and 3b on NCDs, while giving due regard to managing conflicts of interest.
2. Invite the private sector to strengthen its commitment and contribution to the implementation of national responses to prevent, control, and treat NCDs to reach health and development objectives by contributing to further improving access to and the affordability of safe, effective, and quality in vitro diagnostic medical devices (IVDs), medical devices, medicines and other health products in the prevention and management of NCDs.
3. Strengthen the collaboration between WHO, intergovernmental agencies, and non-state actors in accordance with the Framework of Engagement with Non-State Actors (FENSA) in a meaningful way towards the development of contributions and commitments by the relevant private sector entities to improve access to HPV testing and associated health products for cervical screening.
4. Coordinate and align international partners, including the private sector at the country level, through supporting the development and implementation of appropriate national policies.
5. Develop an approach toward registering, monitoring, and publishing contributions from the relevant private sector entities in the prevention and management of NCDs.

3. Private Sector Considerations for Discussion

At present, there are four Human papillomavirus (HPV) IVDs that are listed by the WHO prequalification programme⁴, which cover both self and provider supported collection. Furthermore, four additional products are currently under assessment. The focus of WHO's Asks to the private sector for commitments on cervical cancer screening is on global commitments and governance structures by companies, with the aim of dramatically improving access to HPV testing and associated health technology products in low-and middle-income countries (LMICs). At the same time, recognizing that many important activities in support of access to HPV testing fall under the responsibility of national governments and other actors, the WHO Asks are directed toward global access policies and activities where the HPV test manufacturers can provide meaningful contributions, such as innovation, quality, procurement, supply chain and affordability.

There are several access barriers that lead to suboptimal uptake of HPV tests in LMICs. These factors indicate both the supply and demand-side of the market. However, through collaborative efforts, the below preliminary WHO Asks could result in considerably improved access to HPV testing.

WHO list of preliminary Asks to the private sector and associated health technology product industry



1. Expand the reach of global access pricing

- 1.1. HPV test manufacturers should extend eligibility for global access pricing, including all-inclusive and/or bundled pricing agreements, to encompass all 132 low and middle-income countries. This eligibility should ensure the inclusion of government agencies and their partners, when such partners are providing services as part of the national program – such as non-profit organizations, third-sector entities, and socially or humanitarian-driven private organizations. Further, there should be consideration for small island developing states and other uniquely challenging country settings as well as private sector health service providers and private sector health insurance firms in low-resource settings. Global access programs should transparently provide information on what is covered in their access pricing, including ex-manufacturer prices of their products including reagents and consumables required as per country income classification level INCOTERMS, service and maintenance requirements, and consumables. Ideally, all-inclusive

⁴ <https://extranet.who.int/prequal/vitro-diagnostics>

and/or bundled pricing models would include maintenance reagents and consumables required and incorporate predefined service agreements (with clear key performance indicators) to assure the quality of testing. (Such after-sales services, however, should not be incorporated in ways that would double-charge customers when the services were already paid for under other contracts, including services with other assay purchases).

- 1.2. HPV test manufacturers should collaborate closely with local distributors to ensure adherence to global access prices domestically. Any mark-ups added by local distributors should be transparent, reasonable, and aligned with the principles of equitable and affordable access to health products. In cases where service and maintenance contracts are not bundled into the price of the reagents, HPV test manufacturers should negotiate affordable and standardized agreements with their local distributors/service agents. These contracts should ensure consistent and reliable support for the equipment.

Challenges addressed: Because of the lack of significant and available funding for national cervical cancer programmes and HPV tests, current costs of HPV Nucleic Acid Technique (NAT) assays remain relatively high, especially compared to simpler testing approaches such as cytology and visual inspection. Transitioning to HPV NAT Assay testing, therefore, has been challenging.

While all of the global access programmes generally include global public sector procurers (e.g. WHO, the Global Fund, UNICEF, etc.), it is sometimes unclear if local implementing partners are included. Stakeholders interviewed in the development of this Discussion Paper also expressed the need for HPV test manufacturers to take proactive measures to educate their local distributors and implement systems to ensure global access prices effectively reach their intended users. This should include transparency in their pricing and making local stakeholders aware of their eligibility for preferential access pricing.

2. Improve domestic (national level) pricing

- 2.1. HPV test manufacturers should make reduced pricing available for all LMICs, allowing for HPV tests and associated consumables/accessories to be more accessible. The volume of reagents purchased by or on behalf of the national programmes should be recognized collectively, including across different pathogens (i.e. HIV viral load, TB, hepatitis C virus viral load, etc.), when NAT assays are purchased from the same company for the same NAT analyser.
- 2.2. HPV test manufacturers should take responsibility for working with their local distributors to identify and address factors contributing to high prices, and to promote fair pricing practices. To the extent possible, HPV test manufacturers should build clauses into existing distributor agreements that allow for the global access prices to be passed onto domestic buyers in the public sector.

Challenges addressed: Reports from various countries highlight a concerning discrepancy in access prices offered to global donors/procurers and NGOs, compared to prices offered by local distributors for government and other local public sector providers. In Latin American countries, for instance, local distributors have been reported to mark up their prices as much as 4 to 5 times the indicated global access price, resulting in high variability in pricing that deters government and other local buyers from switching to HPV testing.

3. Streamline the procurement processes for reagents, consumables, and sample collection devices

- 3.1. Comprehensive supply planning toolkits can assist countries in accurately quantifying their needs for reagents, consumables, and self-collection kits.
- 3.2. HPV test manufacturers should offer – but not require – bundled options that include specimen collection kits and preservation mediums as part of their routine offerings to governments and other buyers. This approach streamlines procurement processes and ensures that essential components are readily available together.

Challenges addressed: Endocervical brushes and specimen preservation medium are required to collect and preserve specimens for HPV NAT assays. While self-collection is widely accepted in many regions, some assays on the market do not have self-collection included in their claimed specimen types available.

Further, only some HPV test manufacturers supply the specimen collection devices and reagents as well as the test kits. The main suppliers of validated specimen collection devices and reagents may have a limited presence in LMICs; may be too expensive; may not maintain sufficient, consistent stock to meet orders and/or may be unvalidated or potentially of lower quality. Some countries have reported that they needed to source specimen collection devices from multiple sources, resulting in different delivery times for the various components, consequently affecting overall testing capacity and availability, and waste of reagents due to varying expiry dates. This fragmentation can lead to poor quality (or no) testing and waste of reagents if not all required commodities are available for specimen collection and testing.

4. Ensure quality assurance of products on the market

- 4.1. Ensure compliance with quality, safety, and performance standards and registration through National Regulatory Authorities, including consideration to participate in the WHO prequalification programme.
- 4.2. HPV test manufacturers should validate and verify additional specimen types that can be used with the assay, focusing on self-collection methods. This ensures flexibility and reliability in specimen collection, particularly in resource-limited settings.

Challenges addressed: A global assessment of commercially available HPV NAT assays revealed 264 distinct HPV assays and 511 test variants (technologically identical assays that target different HPV genotypes)⁵. While this diversity may imply a robust and expanding market, a concerning reality emerges: a significant portion of these assays lack validation for accuracy and reproducibility with 79% without published clinical evidence⁵, regulatory approval (US-FDA, Health Canada, Therapeutic Goods Administration of Australia, Ministry of Health, Labor and Welfare of Japan) or WHO prequalification. Unvalidated assays may be found in private and public health facilities. Further, some assays on the market do not have self-collection included in their claimed specimen types available.

5. Support countries, where the Ministries of Health express interest, to demonstrate that achieving scale up in HPV testing and cervical cancer screening is possible and feasible

- 5.1. The private sector, through close and respectful collaboration with interested Ministries of Health, and in accordance with ethical principles, can inspire more countries to follow suit.

Challenges addressed: To support the case for increased funding for HPV tests and cervical cancer screening, it could benefit the cervical cancer elimination effort to highlight examples of LMICs that have shown a successful pathway to scale-up cervical cancer screening and HPV testing. Private sector actors can play a role in helping interested Ministries of Health to establish those pioneering examples so that

⁵ Poljak M, Valencak AO, Cuschieri K, Bohinc K, Arbyn M. 2023 global inventory of commercial molecular tests for human papillomaviruses (HPV). *J Clin Virol.* 2024 Jun;172, 150671.

governments and donors see an investable opportunity. This scope should be based on core principles which include but are not limited to, sustainable and responsible practices, clear benefit to the global strategy response, and accountable and transparent governance.

Increased advocacy efforts are also necessary to demonstrate the public health and economic value of HPV testing, screening and treatment programmes to decision-makers at the global, regional, national, and subnational levels. Advocacy should also be extended to Ministries of Finance and other important financing stakeholders at the country level.

WHO list of preliminary asks to other actors within the cervical cancer elimination response

6. Enhance political will and advocacy for cervical cancer and HPV testing programmes, both globally, regionally, and nationally.

- 6.1. Global partners and key stakeholders should work closely with national governments to support development of national cervical cancer programmes, and the implementation of policies, plans, and initiatives, including incorporating HPV testing within national budgets and national strategic and laboratory plans.
- 6.2. Global partners and key stakeholders should work closely with national governments to incorporate HPV testing and cervical cancer screening in a patient-centred Primary Health Care (PHC) strengthening approach, including support through domestic resource mobilization and financial protection towards achieving universal health coverage.

Challenges addressed: Cervical cancer screening and HPV testing remains limited across LMICs. While there has been progress in some countries, coverage remains low. For example, only 35% of countries in the Americas have reached the >70% screening coverage target.⁶ Coverage rates in other regions have been even lower. The inclusion of specific cervical cancer targets in national cancer control plans and the implementation of WHO guidelines on cervical cancer screening^{7,8}, with the financial support from governments and donors, would stimulate a large demand for tests. This could render the market for HPV tests in LMICs highly attractive to HPV test manufacturers. However, the uptake today in LMICs is markedly smaller than the need and requires considerable increase in order to achieve the targets set out in the Global Strategy.

7. Increase funding for cervical cancer and HPV testing initiatives, including procurement and programmatic needs

- 7.1. Funders and global partners need to increase funding commitments for the procurement of HPV IVDs (reagents and specimen collection devices), expanding beyond screening within HIV services to reach the general population of women accessing care in the public sector.

Challenges addressed: Despite the presence of national cancer control policies and guidelines for HPV testing in many countries, the translation of these policies into programmatic interventions has been hindered by inadequate funding. To achieve cervical cancer elimination targets, WHO estimates a need for \$10.5 billion in funding between 2019 and 2030 to finance HPV vaccination, screening, and treatment

⁶ Fernandez-Deaza G, Serrano B, Roura E, Castillo JS, Caicedo-Martinez M, Bruni L, *et al.* Cervical cancer screening coverage in the Americas region: a synthetic analysis. *Lancet Reg Health Am.* 2024 Feb; 30: 100689.

⁷ WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention. Available from: <https://www.who.int/publications/i/item/9789240030824>, accessed 11 June 2024.

⁸ WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention: use of mRNA tests for human papillomavirus (HPV). Available from: <https://www.who.int/publications/i/item/9789240040434>, accessed 11 June 2024.

programs in LMICs. Unfortunately, less than \$0.5 billion has been accrued, with the majority allocated to HPV vaccination.⁹

8. Provide more predictable volumes for HPV test manufacturers

- 8.1. Large global procurers, along with governments, should collaborate to coordinate their procurement volumes. Joint negotiation, group contracting, and demand aggregation with HPV test manufacturers can leverage economies of scale and ensure more favourable unit prices and lower transactional costs. In cases where joint tendering with foreign entities is not feasible, collaborative efforts can align procurement forecasts and information.
- 8.2. Procurement entities should share accurate and up-to-date procurement forecasts with HPV test manufacturers on an ongoing basis. This transparency is crucial for HPV test manufacturers to anticipate demand accurately and plan their production and supply chain operations effectively to ensure the security of supply.
- 8.3. Governments and key stakeholders are encouraged to take proactive steps to identify gaps in the market and country ownership in the procurement and distribution processes, including safeguards against the risk of substandard or falsified products entering the market.

Challenges addressed: Fragmented and inconsistent ordering and volume calculations that do not reflect actual procurement intentions can lead to delayed production, short shelf-life upon delivery, higher prices, delayed order fulfillment, and other challenges. Improved demand aggregation should be addressed and is one of several collaborative buyer approaches to more strategically source HPV tests for screening. Information sharing, informed buying, coordinated procurements and tiered pricing are all methods that can also contribute to the rationalization of procurement processes, reduce unit and procurement transaction costs, and better ensure the reliability of HPV tests.

9. Increase access to HPV IVDs, through improved demand generation and case-finding

- 9.1. Governments, donors, and partners are encouraged to invest in demand-generation activities to raise awareness of cervical cancer and the benefits of screening. This includes targeted campaigns and community engagement efforts in regions with low awareness.
- 9.2. Governments, donors, and partners are encouraged to collaborate closely with other disease programmes, including HIV and tuberculosis, to ensure HPV testing is incorporated in diagnostic integration efforts, particularly in sharing devices and services (ie. Specimen transportation networks, human resources, service and maintenance, etc.) required and generally already in place for NAT needs across programmes. This will create optimized, integrated diagnostic networks and services that best serve country programmes to tackle all diagnostic system needs, removing the oftentimes siloed programmatic and diagnostic services, while ensuring access to critical diagnostics less well-resourced.
- 9.3. Governments and partners are encouraged to execute diagnostic network optimizations in countries where they have not been performed to provide valuable insights into existing testing platforms' utilization rates and spare capacity for HPV testing. This optimization helps maximize the efficiency of testing infrastructure and resources.

Challenges addressed: The implementation of the WHO guideline on cervical cancer screening and treatment, supported by financial backing from governments and donors, would stimulate a large demand for testing and could render the market for HPV tests in LMICs highly attractive to HPV test manufacturers.

⁹ TogetHER for Health. Investing in Global Cervical Cancer Prevention: Resources for Low-Income and Lower Middle-Income Countries in 2021. 2022.

However, the uptake today in LMICs is markedly smaller than the need^{10,11}, which in part appears to diminish the interest of HPV test manufacturers and local distributors to invest in demand creation and other market development activities. Demand generation, case-finding, and outreach amongst the general population could considerably increase access to cervical cancer screening, thereby increasing the volume of HPV tests.

Additionally, there remains limited awareness of cervical cancer and the overall benefits of HPV testing contributes to women not actively requesting HPV tests from their healthcare providers. Moreover, when cervical cancer screening is offered, healthcare providers can only prescribe those test modalities that are available at their clinics, or what they know and are comfortable with – oftentimes, this is cytology or visual inspection. This may contribute to a cycle of limited demand for and access to HPV tests. Where HPV tests are available, turnaround times for test results can be slow, limiting access and eroding trust. Furthermore, cervical cancer screening and treatment measures are often not readily available in primary healthcare facilities – the place where most patients seek care first. There is an urgent need to scale up community initiatives to educate women about the seriousness of cervical cancer and decentralize testing to increase cervical cancer screening rates in all settings.

Additionally, national HIV and TB programmes, as well as emergency response programmes, have made substantial investments in NAT analysers, including developing systems more streamlined across disease programs and less siloed. Many of these same devices and systems include HPV assays and/or could incorporate HPV tests into the system (ie. specimen transportation, human resources, data management, service and maintenance) in improve efficiencies, ensure access, and lower costs. While some countries have successfully integrated cervical cancer programmes into existing diagnostic capacity and workflow, leveraging established systems and reducing upfront costs, this approach is not universal. Furthermore, some cancer programmes have established their own diagnostic system instead of prioritizing integration with other programmes. Advocacy and support from the MOH and other partners will be crucial for developing clear policies to optimize the incorporation of HPV into diagnostic integration efforts.

4. Conclusion

Improving access to HPV tests and associated health products for the screening and diagnosis of cervical cancer is complex yet critical. Interventions require collaboration and commitment for greater impact at the country level. Through the NCD private sector dialogues, WHO will work across programmes and with partners to support countries to mobilize resources and accelerate structural transformations that together will support the scale-up of HPV tests and associated health products as well as the inclusion of cervical cancer screening, prevention, and treatment in primary healthcare and universal health coverage packages. This multisectoral approach represents a valuable opportunity to build stronger collaborations, as well as partnerships between governments, care providers, patient advocates, non-governmental organizations and other relevant stakeholders, as we move toward ensuring access to HPV testing for cervical cancer screening.

¹⁰ Mungo C, Orang'o O, Ofner S, Musick B, Yiannoutsos C, Cohen CR, *et al.* Real-world cervical cancer screening uptake and predictors of visual inspection with acetic acid positivity among women living with HIV in care programs in western Kenya. *JCO Glob Oncol.* 2024 Feb;10:e2300311.

¹¹ Yimer NB, Mohammed MA, Solomon K, Tadese M, Grutzmacher S, Meikena HK, *et al.* Cervical cancer screening uptake in sub-Saharan Africa: a systematic review and meta-analysis. *Public Health.* 2021 Jun;195:105-11.

Disclaimer

The World Health Organization (WHO) welcomes views from all participants prior to, during, and after the Dialogue to be held on 25th and 26th June 2024. This discussion paper should be viewed as a work in progress developed to support the objectives of the meeting. It encourages inputs, commitments, and contributions from the private sector and associated health technology product industry to support WHO's activities to strengthen and improve access to diagnostics and related health technology products for cervical cancer. The private sector's input will be collected through the dialogue. As a discussion paper, this document serves as a starting point for dialogue, rather than a definitive assessment.

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