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Area for Intervention:

Accelerate access to tools to drive Elimination of Mother-to-Child Transmission (EMTCT) of HIV, syphilis, and hepatitis B, including Chagas in endemic areas

HIV/coinfections Programmatic Priority: Increase access to screen and treat for cervical cancer and sexually transmitted infections

For Information For Review and Advice For Decision

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1. Purpose of this document

This Area for Intervention (Afi) outlines a priority investment opportunity, focusing on improving access to tools to drive elimination of mother-to-child transmission (EMTCT) of HIV, syphilis, and hepatitis B (and Chagas in endemic areas), for Executive Board endorsement.

2. Introduction

In response to Unitaïd’s Programmatic Priority to increase access to screening and treatment for cervical cancer and sexually transmitted infections (STIs), as well as a **recent surge in momentum behind the global EMTCT agenda**, there are **compelling opportunities to accelerate EMTCT of HIV, syphilis, hepatitis B – and Chagas** in endemic areas.

The vision for “**Triple Elimination**” is grounded in evidence demonstrating that linking interventions for HIV with services for other sexually transmitted infections, including syphilis and hepatitis B virus (HBV), improves uptake and optimizes the use of limited resources. The three diseases share many features, including epidemiology, routes of transmission, and interventions that exist to address them. In regions where Chagas is endemic, the Triple Elimination agenda is expanded to include congenital Chagas (‘EMTCT Plus’). The urgency to act is underpinned by the significant morbidity and mortality caused by MTCT of these diseases in low- and middle-income countries (LMICs) and the underutilization of lifesaving tools. **The burden of transmission is heavily skewed towards underfunded health systems, where promising interventions have the highest potential.**

Unitaid is well placed to make a difference in this area, drawing on longstanding expertise in HIV and co-infections as well as a rich portfolio of grants that target pregnant women and infants. The opportunities to advance the EMTCT agenda align well with other programmatic priorities on safe pregnancy and birth for women and newborns, and on integrated diagnostics. Unitaid’s published landscapes were critical to defining relevant opportunities in this area, including landscapes on [innovative tools and delivery strategies for eliminating vertical transmission of HIV, syphilis, hepatitis B, and Chagas in endemic areas](#) and on [screening and treatment for Chagas disease](#). Unitaid has included efforts to accelerate adoption and integrated delivery of tools for EMTCT as an opportunity in the 2024 baseline of the Investment Plan. Efforts to provide catalytic product development support to advance key diagnostic priorities are also included in the 2024 upside, and both opportunities represent strong investment prospects for Unitaid.

3. Public health burden and key access issues

While EMTCT has significant potential for global health impact, progress has been slow. The global response is significantly off-track in meeting WHO targets, with the gains in reduction of vertical transmission of HIV not realized for syphilis, HBV, and Chagas disease.

The burden of congenital syphilis is the largest and the area in which EMTCT interventions have the highest potential to save lives. Although more than 90% of countries have policies for antenatal screening and treatment, the high rate of congenital syphilis (estimated at 473 cases per 100,000 live births), demonstrates that large gaps in screening and treatment remain – far below the 2030 elimination target of 95% of pregnant women screened for syphilis, and over 95% of syphilis-seropositive pregnant women receiving effective

treatment in 70% of countries. In 2016, an estimated 1 million pregnant women worldwide had active syphilis infection, resulting in approximately 355,000 adverse pregnancy outcomes, including 206,000 stillbirths or neonatal deaths, with almost 60% of adverse outcomes occurring in Africa. **In the first four weeks of life (neonatal period), syphilis is a greater cause of death than malaria and diarrheal diseases, and is now a greater cause of global child mortality than HIV.**

The WHO global hepatitis strategy aims to reduce new chronic HBV infections by 90%¹ and to achieve a 65% reduction in HBV-related deaths through improved diagnosis and treatment. Although many countries are on track to achieve the first target, there is significant geographic variability. The number of **new neonatal HBV infections has remained roughly unchanged globally despite large reductions in infant infections achieved through vaccination.** Chronic HBV infections cause approximately 820,000 HBV-related deaths annually. **Mother-to-child transmission of HBV during delivery is the most common timepoint for infection.** Deaths from HBV typically occur later in life, reducing lifespan among affected individuals from hepatic cellular carcinoma and liver cirrhosis. The burden of HBV is geographically dispersed with highest burden in the African and Western Pacific regions.

The global HIV target is to eliminate new infections in children by 2030. This will require a 10-fold reduction in new cases from the 2020 baseline. **While prevention of MTCT of HIV has been a noteworthy achievement, progress has varied, and new HIV infections among children still reached 150,000 in 2020,** with about half occurring in East and Southern Africa. Despite widespread scale-up of antiretroviral therapy (ART), 680,000 people died from HIV-related causes and 1.5 million acquired HIV in 2020. Every year, an estimated 1.3 million women and girls living with HIV become pregnant and without intervention the rate of transmission to children during pregnancy, labour, delivery or breastfeeding ranges from 15% to 45%.

For Chagas, included under 'EMTCT Plus' where the disease is endemic, PAHO has set targets for EMTCT, including 1) increasing testing of pregnant women to more than 90%, 2) increasing testing of neonates with seropositive mothers to more than 90%, and 3) increasing treatment of seropositive mothers to more than 90%. **MTCT of Chagas disease is estimated to cause about 9,000 new cases in newborns in Latin America annually.** Despite growing advocacy efforts, Chagas disease programs are underfunded, and uptake of existing diagnostics remains low and less than 1% of the 6 to 8 million people currently living with Chagas disease are estimated to be receiving treatment.

4. Potential opportunities to improve access to lifesaving tools for EMTCT

There are concrete, actionable opportunities to support adoption of optimal packages of interventions for accelerating Triple Elimination drawing on newly available and underutilized tools. These packages will need to be tailored to incidence levels and the maturity of the response, which vary between settings. It is an opportune time to intervene as countries now have access to the guidelines, tools, and funding needed to make EMTCT possible, as well as strong leadership and political will reinforced by WHO and PAHO's elimination agendas. In the last several years, WHO has published extensive normative guidance, including on HBV testing (2017); use of antiviral prophylaxis for treating HBV in pregnancy (2020); guidelines for diagnosis and treatment of Chagas disease (2019); consolidated HIV testing guidelines (2019) recommending

¹ as evidenced by HBsAg prevalence in children <5 years of <0.1% by 2030

the dual HIV-syphilis rapid diagnostic test (RDT) as the first screening test in the antenatal care algorithm; and combined guidance for validation of EMTCT for HIV, syphilis, and HBV (2021).

Tools and interventions are available, but there are key gaps in their use and implementation. Newly available rapid diagnostic tests could detect infections during pregnancy and breastfeeding and support linkage to care. Previously, syphilis screening was reliant on complex laboratory-based tests that limited access. Among the global adverse birth outcomes related to maternal syphilis infection, 57% occurred in pregnant women who attended antenatal care but were not screened for syphilis and 16% occurred in mothers who were screened but not treated. HBV screening in antenatal care is even lower, with screening coverage at less than 20%. New tests – including single and dual HIV/syphilis RDTs and hepatitis B surface antigen (HbsAg) RDTs – could close these gaps and save lives. These efforts can also leverage a new volume guarantee for SD Biosensor’s STANDARD Q HIV/Syphilis Combo test that reduces the price to US\$0.95.

In some cases, supply and delivery barriers need to be addressed to ensure access to treatment and antiviral prophylaxis for pregnant women following diagnostic testing in antenatal care. Congenital syphilis can be averted with one dose of long acting benzathine penicillin G (BPG). Following global shortages of BPG between 2014-2017, however, the market remains fragile, with quality issues, low margins, fragmented demand and country-level supply and delivery issues. And although low-cost generic tenofovir is available, access is limited for patients who need it for HBV antiviral prophylaxis, and demand forecasting tends to focus on HIV only.

Evidence generation on impact, feasibility, and cost-effectiveness would accelerate demand and adoption of EMTCT products and strategies. Pilot implementation and monitoring of integrated programs can help overcome challenges in coordination between HIV, STI, MCH and hepatitis programs to avoid fragmentation of services. Targeted advocacy activities will also be critical, including community-led demand creation and diagnostics and treatment literacy.

Service delivery innovations could facilitate more rapid, consistent, and equitable access to tools and interventions for EMTCT. These include integrated approaches such as bundling delivery of essential diagnostics in ANC and targeted behavioral interventions to drive adoption and save time and costs for patients and health systems, through streamlined procurement, simplified training, reduced unit costs, and rapid results and treatment.

For example, a key opportunity is to improve coverage of the Hepatitis B birth dose (Hep-BD), a recommended vaccination that should be delivered within 24 hours of birth. It is the most effective PMTCT option for HBV, but HepB-BD coverage is less than 10% in Africa, where the high proportion of home-based deliveries hinders access. HepB-BD has not been part of the vaccines supported by Gavi because the price (US\$0.20) is below the minimum country co-financing level for low-income countries. However, in 2018 Gavi approved support for the introduction of HepB-BD but delayed implementation due to Covid-19. If Gavi’s support is re-confirmed, then there are opportunities for a collaboration to support countries to identify effective delivery models to overcome adoption barriers, particularly at the community-level and for home births.

Finally, new product development could complement efforts to improve access to existing and emerging tools. A low-cost point-of-care HBV viral load test and a device-free point-of-care HIV test could be transformative, enabling test-and-treat algorithms even in remote settings and for the most vulnerable.

5. Partner engagement

The World Health Organization spearheads the global Triple Elimination agenda with WPRO and PAHO regional offices leading development and implementation of regional EMTCT frameworks. Civil society groups are also a critical voice in support of Triple Elimination such as the World Hepatitis Alliance. Other stakeholders include a strong network of implementers – many having historically supported EMTCT of HIV but adding syphilis and HBV more recently. For Chagas, there are opportunities to leverage investments by bilateral donors and build on regional initiatives in the Americas.

New announcements from key scale-up partners significantly strengthen the scalability pathway for these products. Global Fund has recently announced the eligibility of Triple Elimination interventions for the 2023-2025 allocation period in its Modular Framework Handbook, including activities related to integrated testing for HIV, syphilis, and hepatitis B among pregnant women and linkages to treatment. PEPFAR is funding implementation of all PMTCT services for HIV, including use of dual HIV/syphilis tests in antenatal care, and supports national EMTCT strategies. While PEPFAR does not currently fund syphilis treatment or HBV testing and care, they are supportive of Unitaid’s engagement in this space and would consider implementation evidence to inform decisions around expanding EMTCT support. UNICEF has identified effective integration of HIV interventions in primary healthcare services as a key strategic priority and will support countries towards Triple Elimination. These recent announcements offer the potential to leverage donor-financed procurement volumes within implementation pilots.

Gavi’s Executive Board will take a decision on whether to reconfirm support for introduction of the Hep-BD in June 2023. If the support is greenlighted, then Gavi has expressed interest in collaborating around a learning agenda for Hep-BD roll-out, including how best to deliver these vaccinations in remote facilities and at the community level. This presents an opportunity to define new partnership models for Unitaid and Gavi that include catalytic implementation research investments by Unitaid that lay the foundation for broader scale-up by Gavi.

Coordination and joint planning at global and national levels will be essential to advancing EMTCT and Unitaid is well placed as a convenor and pathfinder to drive forward this critical agenda. Consulted partners showed strong and consistent enthusiasm for Unitaid’s potential leadership in this space.

6. Opportunities for Unitaid investment

6.1. Implementation work to accelerate demand and adoption of new and underutilized EMTCT commodities as part of integrated national strategies

Large scale, multi-country implementation pilots are needed to drive adoption of EMTCT commodities and newly launched WHO guidelines. Evidence on impact, feasibility and cost-effectiveness can support national adoption of integrated and locally tailored EMTCT programs and strategies. This would inform national programming in a way that overcomes traditional disease silos and maximizes the overlap between tools and platforms. Targeted advocacy activities with and by community and civil society groups are critical to building

demand. Context-specific optimal packages of EMTCT interventions would leverage newly available and quality-assured single and dual HIV/syphilis RDTs and HBV surface antigen (HBsAg) RDTs to quickly identify women at risk of vertical transmission and facilitate linkage to care. In Chagas endemic regions, packages would incorporate Chagas technologies to strengthen treatment access, including new molecular platforms. Packages may also include self-care products and approaches to improve access. Implementation work could also inform opportunities to address global- and country-level supply and delivery challenges related to availability of quality-assured and affordable BPG and tenofovir, leveraging procurement volumes and improving demand forecasting to avoid supply disruptions. For countries introducing the HepB-BD, evidence generation on targeted roll-out strategies, including for out-of-facility births, could catalyze greater uptake and complement GAVI's implementation support. Data generated from Unitaid work could also inform further WHO implementation guidance.

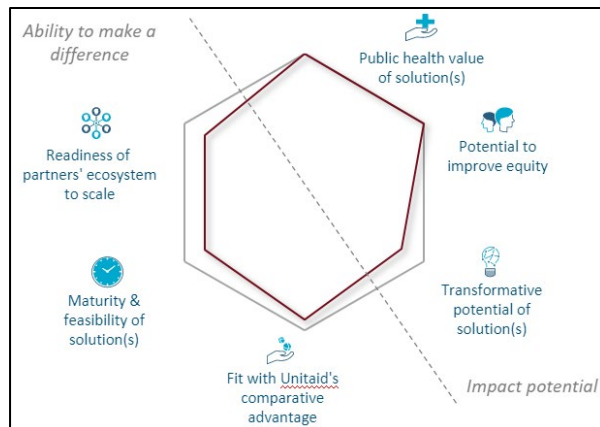
6.2. Catalytic product development support to advance key diagnostic priorities (e.g. point-of-care HBV viral load test, device-free point-of-care virologic test for HIV-exposed infants).

Future diagnostic tools could be transformative in enhancing equity by closing the testing gap for the hardest to reach populations. The biggest product development gap identified is the lack of POC HBV viral load tests, which hinder access to treatment. Current guidelines recommend HBV viral load testing following a positive HBsAg RDT result to guide antiviral prophylaxis treatment decisions, but these tests are often inaccessible due to their complexity and high cost. Another product development opportunity that may expand testing access, particularly for HBV, is development of a multiplex RDT for HIV, syphilis, and HBsAg. Use of the HIV/syphilis RDT has demonstrated how the addition of a dual test to an existing ANC screening platform can rapidly increase coverage of the added test. In regions without strong existing ANC testing platforms (e.g., West and Central Africa), a low-cost multiplex test could potentially serve as the impetus for re-invigorating PMTCT programs. A further transformative solution would be development of a simple, accurate, and device-free POC virologic test for HIV-exposed infants. This test could also be used in other non-PMTCT settings (e.g., malnutrition clinics, tuberculosis clinics, inpatient paediatric wards) that are high-yield for case finding. WHO has suggested that even with lower sensitivities, this test could provide added value to programs and substantially affect the morbidity and mortality of HIV-exposed infants. A Unitaid investment to develop, validate, and bring to market POC tests that fulfil these needs could have high impact and expand testing access.

The opportunities proposed in Section 6 align with all three Strategic Objectives (SO) of Unitaid's Strategy 2023-2027 and particularly with SO1.

7. Assessment of the opportunity

7.1. Impact potential, including public health value of the solution, potential to improve equity, and the transformative potential of the solution



Using the prioritization criteria, the EMTCT implementation work opportunity shows strong potential impact, with a high estimated public health value and potential to improve equity, and moderate transformative potential. If the product development opportunity in the upside were included, the scoring for transformative potential would increase.

For the implementation opportunity, early adopter countries provide an indication of potential impact. In Uganda, efforts to scale-up the dual HIV/syphilis RDT

led in an increase in syphilis screening in ANC from 48% to 94%. Globally, modelling commissioned by Unitaid found that bringing syphilis screening rates up to HIV screening rates would avert 129,000 cases annually, preventing 32,000 stillbirths, and 10,000 neonatal deaths per year by 2030, while universal scale-up could prevent 128,000 stillbirths and 45,000 neonatal deaths each year in the same time frame. The potential impact of universal scaling of Hep-BD and HBV testing and antiviral prophylaxis could avert around 160,000 chronic cases in 2030. GAVI's impact modelling found that their introduction of the Hep-BD between 2021-2035 could avert between 0.3 – 1.2 million deaths (excluding Nigeria). The product development opportunity scores comparatively lower for impact. Unitaid modelling found that introduction of a device-free infant HIV viral load POC test could result in 36,000 additional HIV+ infants receiving an early diagnosis, which could prevent around 8,700 premature deaths in the year 2030. This would mean the intervention could avert around 11.5% of the current deaths from HIV/AIDS among 0–4-year-olds.

From an equity perspective, improving access to testing and care through antenatal/postnatal care platforms will support those presenting at lower-levels of the health system and for babies born outside of health facilities. Efforts to decentralize access to these services will directly benefit high-risk, marginalized populations. Equity is equally high scoring for both opportunities.

The transformative potential of the tools lies in their ability to leverage the gains in HIV, by bringing syphilis, HBV and Chagas services to unreached populations. These increases in coverage are complemented by efficiency gains, including potential for same-day treatment. For the product development opportunity, availability of a point-of-care HBV viral load test will enable rapid and accessible testing and care after a positive HBsAg result, and a device-free viral load test for HIV-exposed infants could further decentralize testing access.

7.2. Ability to make a difference, including fit Unitaids comparative advantage, maturity and feasibility of the solution and readiness of partner ecosystem

Both opportunities are well-suited for Unitaid to make a difference, with a close fit with Unitaids comparative advantage. The implementation opportunity has stronger maturity and feasibility than the product development opportunity, but both demonstrate robust readiness of the partners' ecosystem. The

proposed activities to accelerate uptake of technologies and product development are both core strengths of Unitaid. Unitaid has longstanding expertise and proven success in expanding access to HIV diagnostics and treatment, as well as integrated delivery of diagnostic tools, including multi-plex diagnostic platforms. It also has synergistic work on eliminating congenital Chagas through improved detection and treatment of mothers with Chagas disease and newborns. The opportunities would build on existing platforms, and many of the new RDTs are already commercially available, with registration commencing in several countries. Opportunities to leverage forthcoming investments in multiplex diagnostics could also strengthen Unitaid's product development priorities and accelerate the impact of efforts in Triple Elimination. Tenofovir is available as well, including from several generic and prequalified suppliers. Efforts to streamline procurement and integrate products within national guidelines are now needed. Regarding the partner ecosystem, the opportunity is well aligned with WHO's 2022 Global Health Sector Strategy on HIV, viral hepatitis and STIs, which calls for integrated efforts to advance Triple Elimination. While the scale-up environment is more difficult for STI products and services, there are opportunities to leverage funds from PEPFAR and the Global Fund. Given that the maternal and newborn health funding landscape is more fragmented, increased efforts to support transition to scale will be needed, including engagement to mobilize domestic financing.

7.3. Risk

The opportunity has a low-moderate risk profile. Strategic risks are low given the high public health value of the opportunity and its strong fit with Unitaid's comparative advantage. There is strong alignment among stakeholders on the need for catalytic action on Triple Elimination and for Unitaid's leadership to take this forward. Implementation risks are medium-low given the strong partner ecosystem and key implementers with well-established capacity in this area. There are potential challenges related to the complexity of integrated interventions, however, even with buy-in across vertical disease program stakeholders. Scalability risks are medium, given that the scale-up environment is more difficult for STI products and services, but there are opportunities to leverage support from the Global Fund, PEPFAR and GAVI. However, these partner support announcements are new and the funding landscape is more fragmented, thus increased efforts to support transition to scale will be needed, including engagement to mobilize domestic financing. The scalability risks are comparatively higher for the Chagas products and measures to ensure implementation sustainability would be a key focus of any future investment.

7.4. Cost and level of effort

A moderate investment (US\$ 25-30m) would be required to fund the proposed implementation work, and a smaller investment (US\$ 15-20m) for the product development component. The Secretariat expects to be able to deliver the interventions within a budget of US\$ 25m if undertaking the implementation work only, with an upper-bound of US\$ 45m if including the product development work.