Unitaid
SAVE LIVES FASTER

44th Executive Board Meeting
18-19 June 2024
The Forum, Global Health Campus
Geneva, Switzerland

Agenda item 9

Area for Intervention:
Regional Manufacturing for Equitable Access (RMEA)

Programmatic Priorities: *Cross-cutting technologies & topics*
Strategic Objectives: *Create systemic conditions for sustainable, equitable access*

For Information ☐ **For Review and Advice** ☐ **For Approval** ☒

Contents

1. Purpose and context of this document

Unitaid's Executive Board (EB) adopted the organizational strategy for the 2023-2027 period during its 40th meeting held in June 2022. The strategy, with a vision to achieve "equitable access to health innovations to ensure healthy lives and promote wellbeing for all," highlighted as its second strategic objective, the need to "create systemic conditions for sustainable, equitable access." This strategic objective encompasses established areas under Unitaid's mandate, such as the facilitation of an enabling environment for access (including intellectual property and regulatory systems) and seeks to consolidate Unitaid's efforts to support innovative supply models and approaches, including strengthening the sustainability of interventions through regional manufacturing of health innovations.

In June 2023, the Executive Board, through its Resolution "UNITAID/EB42/R3", approved the immediate implementation of Phase 1 of the Secretariat's functional review, including implementation of areas of work strengthened in the strategy, including **"Regional Manufacturing for Equitable Access" (RMEA)**. The pre-implementation activities approved through this Resolution have since been ramped up, and, as a result, the Secretariat has mapped out RMEA opportunities for transformational impact. The Secretariat has estimated funding requirements (specified and core funding) to implement a first phase of interventions in this area and seeks the guidance of the Executive Board on the RMEA approach and the identified interventions.

As presented by the Executive Director at EB42, RMEA is not new to Unitaid, as it is an integral part of Unitaid's Access approach and toolbox. Moreover, investment opportunities for a first wave of interventions under the RMEA cross-cutting Area for Intervention (AFI) will be taken forward in line with existing product/programmatic priority AFIs. One such investment opportunity is embedded in the package recently approved by the Executive Board through resolution n°11-2024-e: "Acceptance of a Specified Contribution from the European Commission and expansion of investments in new tools to reduce maternal mortality." This includes an objective to *"Improve access to affordable quality-assured recommended commodities to prevent and treat PPH in Africa, especially through manufacturers in Africa."*

This document presents Unitaid's overall approach to RMEA, which includes strategic prioritization of products in Unitaid's 30 by 2030 target pipeline, evaluation of the potential for commercial viability and impact through the development of business cases for these products, and design of interventions best suited for Unitaid. The document is provided as an Area for Intervention (AFI) in line with Unitaid's operating model. However, this AFI has been written to contain more details than the standard AFI; this is done exceptionally to accommodate additional details that may be required by the Executive Board for a new Strategic Initiative.

2. Introduction

Equitable access to affordable, context-specific, quality-assured health products is crucial for the success and sustainability of public health programs and Universal Health Coverage (UHC). Given challenges related

to trade, quality, and other relevant regulations, dependence on imported health products has significant potential to threaten the achievement and sustainability of equitable access goals of public health programs in LMICs, including health emergency preparedness and response. The COVID-19 pandemic and the inequities of access for LMICs to vaccines, therapeutics, diagnostics, and other health products to respond to the pandemic reignited attention and support for greater health security, access independence, and socioeconomic development through regional manufacturing of health products.

Multiple initiatives towards strengthening regional manufacturing of health products were launched by governments and regional and continental institutions across Africa and Latin America in reaction to the challenges faced during the pandemic. However, while the pandemic amplified and introduced increased urgency of the regional manufacturing agenda, there are several examples from before the pandemic where support - including through Unitaid - for improving the quality and affordability of products manufactured in Africa and Latin America were identified as impactful supply-side access interventions. As such, the foundation for accelerating and deepening engagement in this area exists and is expected to provide a strong platform from which to launch additional new interventions.

Africa and Latin America as priority regions for Unitaid's RMEA AFI

LMICs (Low- and Middle-Income Countries) have the largest gap in health products manufacturing capabilities. **Africa, for example, imports over 70% of finished pharmaceutical products (FPP) and over 95% of Active Pharmaceutical Ingredients (API).** However, indigenous manufacturers have been found to have the widest reach in many African countries. Furthermore, these manufacturers are better positioned to maintain market continuity of diagnostics, medicines, and vaccines unique to the population in the region. Many indigenous and African-owned manufacturers on the continent are committed to manufacturing according to global current Good Manufacturing Practices (cGMP), evidenced by the growing number of contract manufacturing agreements on the continent and a few manufacturers already having achieved WHO prequalification for selected products.

Unitaid's approach to regional manufacturing:

- ✓ Unitaid is one of the organizations that actively promotes a regional approach to health products manufacturing, with an emphasis on building regional value chains that seek to meet the specific healthcare needs in respective regions.
- ✓ WHO and some other stakeholders still use the term "local manufacturing", but there is a major alignment that this is not synonymous to national. For example, in the context of Africa, the definition of "local" is extended beyond domestic (national or subnational) to regional and continental i.e., within the territory of the member countries of the African Continental Free Trade Area.
- ✓ Manufacturing of health products can be defined as all activities, including some or all value-added manufacturing operations, leading to the production of the respective health products. These include the synthesis of API, antigens or antibodies and other constituents of in-vitro diagnostics, and final formulation of finished pharmaceutical and diagnostics products.

Similarly, there are few manufacturers of In vitro diagnostics (IVDs) in Africa with manufacturing facilities that comply with ISO 13485 and other quality certifications. However, the health manufacturing sectors in most African countries continue to trail their global peers, with almost all manufacturing inputs (such as APIs, antibodies, and adjuvants) being imported and little or no manufacturing of high-tech products like specialized formulations of small molecules, biologics (including vaccines), and the critical inputs for rapid and molecular diagnostics. To address these challenges, in 2007, the African Union Development Agency (AUDA-NEPAD) developed the Pharmaceutical Manufacturing Plan for Africa (PMPA). This business plan proposes a package of technical solutions to catalyze production of pharmaceutical products in Africa to ensure access, quality, availability, and affordability of pharmaceutical products. AUDA-NEPAD also

provides oversight on a pathway for diagnostics manufacturing and regulatory systems strengthening through a regional partnership with the Africa CDC.

The state of health products manufacturing in Latin America is characterized by a multifaceted landscape influenced by economic factors, regulatory frameworks, and healthcare infrastructure within individual nations. Access to essential medicines and health technologies in the region is complex, necessitating safety, quality, affordability, and timely availability considerations. Although domestic and foreign companies in Latin America supplied over 50% of the market through manufacturing in the region, including through the leadership of countries like Brazil, the region still experiences significant challenges with access to innovative health products. The PAHO 59th Directing Council's endorsement of the policy document "Increasing production capacity for essential medicines and health technologies" underscores the collective effort to enhance manufacturing capabilities in the region. Before the pandemic, several Latin American and Caribbean countries experienced a rise in domestic pharmaceutical and medical device production. However, the region remains challenged with access to many innovative medicines (often due to IP barriers); the region also imports most of its APIs, contributing to its access challenges.

What are the key issues, why now, and why Unitaid?

The success of global health efforts towards UHC and pandemic preparedness, planning, and response hinges on equitable access to affordable, context-specific, quality-assured, low–carbon, and climate–resilient health products.

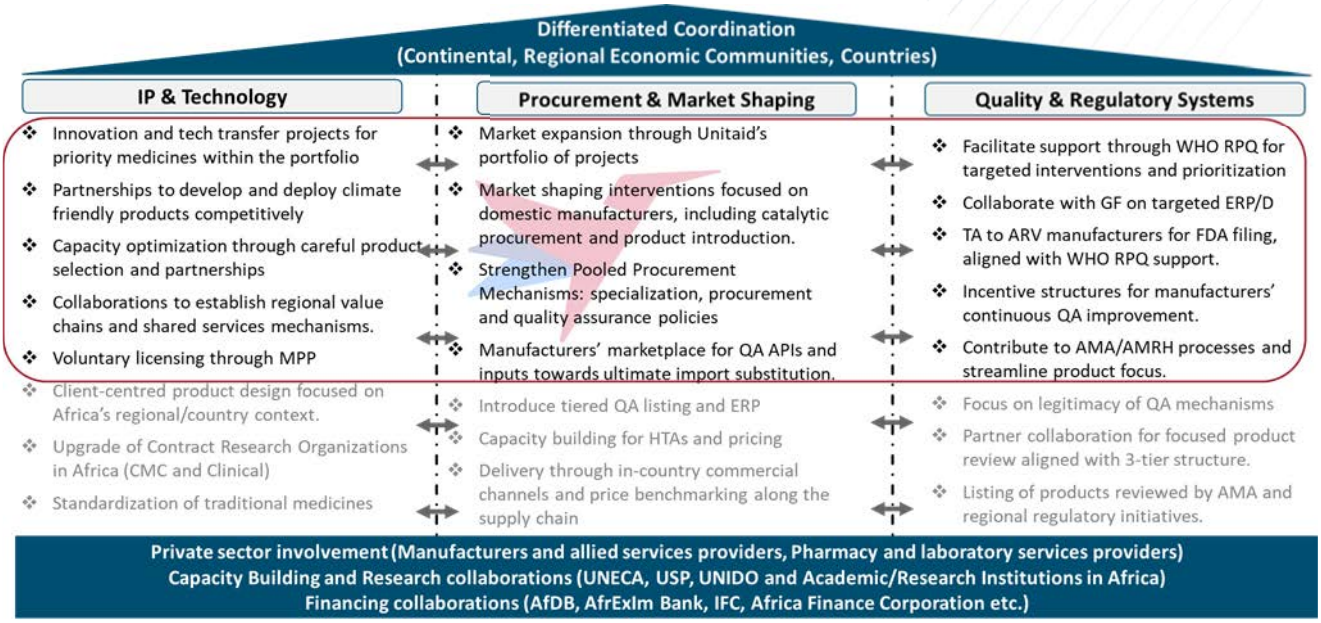
The current proliferation of nationalistic approaches and strategies for local production of health products by governments in reaction to the commodities' supply challenges faced during the COVID-19 pandemic has the potential to lead to fragmentation of markets and run counter to equitable access objectives. An irrationally fragmented and poorly coordinated supply landscape can potentially increase cost and quality concerns for essential health products required for the global health response and UHC. Furthermore, poor coordination could lead to several lost opportunities to build capacity and expand capabilities required for pandemic preparedness, leaving the same regions that were vulnerable during the COVID-19 pandemic in a similar (and possibly worse) situation in the event of another pandemic. Finally, major environmental sustainability challenges within the current value chain of health products require deliberate action to minimize the impact of health value chains on the climate.

The shrinking fiscal space in the global health response, the need to build resilient and agile health systems that are positioned to effectively respond to existing and future pandemics, and the need to acutely reduce the impact of health value chains on the climate create an urgency to act decisively on critical enablers of innovative and sustainable supply models. In addition, the recent calls to action, such as the Yaounde "Declaration for accelerated reduction of malaria mortality in Africa" and the "Lusaka agenda: Conclusions of the future of global health initiatives process," have been unequivocal on the need for urgent action for a speedy and coordinated approach to accelerating regional manufacturing as an enabler to equitable access. These calls by governments, communities, and global health actors describe the need for catalytic pathfinder investments to set this agenda in the right direction.

Unitaid's roles as pathfinder, influencer, and investor in facilitating equitable access to health products are well recognized globally. The Lusaka agenda, for example, tasked Unitaid and other global health agencies to "convene a process to establish a vision for a more coordinated approach to R&D, manufacturing, and market shaping." Unitaid is uniquely positioned within the global health architecture to initiate pathfinder investments that will help catalyze the overall approach of regional manufacturing for equitable access for the product classes within our mandate. **Since its inception, Unitaid's work has focused on innovative approaches to facilitate product access, including developing critical capabilities required for strengthening regional manufacturing. Unitaid's portfolio has included support for product/formulation development, quality assurance, and other critical supply-side interventions.** Unitaid has worked with manufacturers across LMICs over the years to improve cost, quality, and market penetration. In addition, Unitaid has undertaken multiple consultations, reflecting on learnings

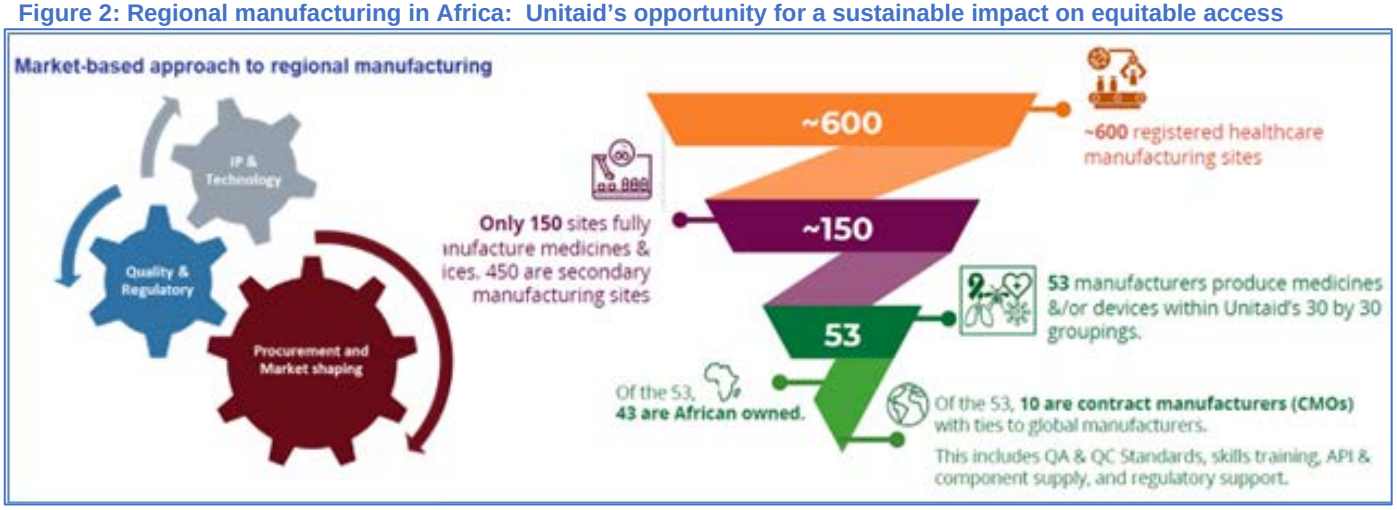
from experience on the subject, which have been deployed to develop a framework for a market-based approach to strengthening regional manufacturing, from which proposed Unitaid interventions have emerged (see Figure 1).

Figure 1: Unitaid's framework for a market-based approach to strengthening regional manufacturing



The product portfolio highlighted within the current Unitaid strategy (30 x 2030) provides ample opportunity for Unitaid's contribution to regional manufacturing for equitable access. The 30 x 2030 portfolio comprises products for which Unitaid will facilitate accelerated introduction and build sustainable markets; hence, suitable candidates where manufacturing such products closer to the point of use further strengthens access. Furthermore, the products are spread across different formulation types and manufacturing platforms, and there are manufacturers within the regions of focus that can manufacture these products at the right quality and cost if given the right support (see Africa example in Figure 2 below).

Figure 2: Regional manufacturing in Africa: Unitaid's opportunity for a sustainable impact on equitable access

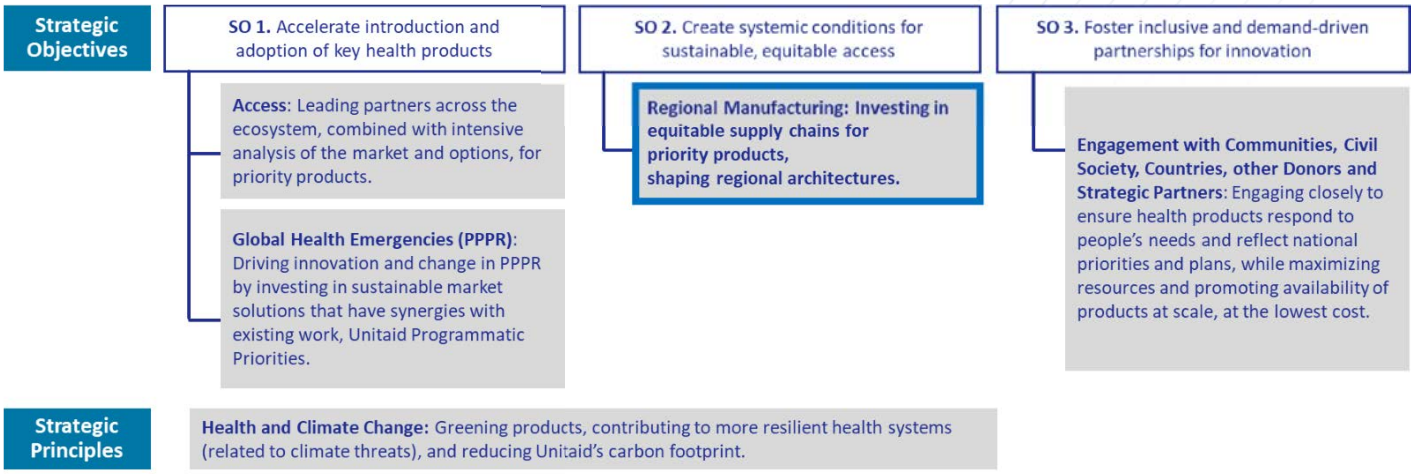


3. Unitaid's 2023 – 2027 Strategy: Regional Manufacturing for Equitable Access AFI

Unitaid's 2023 – 2027 strategy was accompanied by a functional review, which resulted in the reinforcement and expansion of five areas (and the phased approval of additional resources for their implementation)

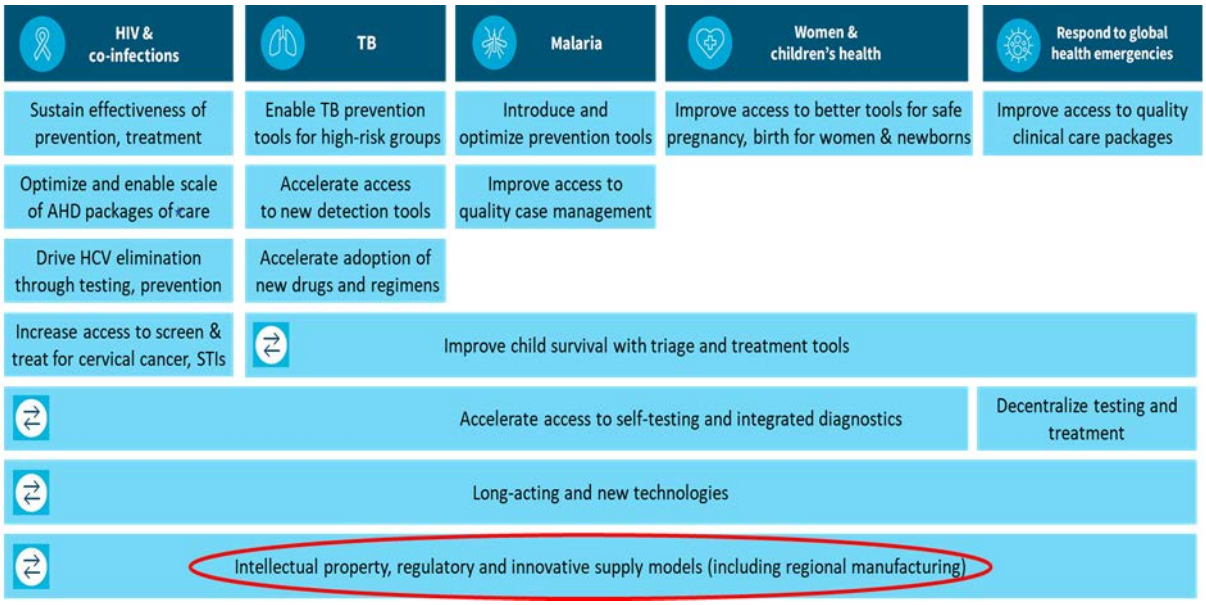
designed to support the delivery of the strategy. These areas, namely Access, Pandemic Preparedness Planning and Response (PPPR), Partnerships, and Regional Manufacturing, are aligned with the new strategy's strategic objectives and principles (see Figure 3 below).

Figure 3: Positioning of the RMEA initiative within the Unitaid Strategy 2023 - 2027



Furthermore, Unitaid's strategy has identified regional manufacturing as a critical cross-cutting AFI that serves as an accelerator and enabler for several other programmatic priorities (product specific and cross-cutting).

Figure 4: RMEA as a cross-cutting programmatic priority (Unitaid Strategy 2023 - 2027)



Following the June 2023 Executive Board meeting, where the five strategic areas mentioned above were approved for expansion/implementation, the Secretariat developed a high-level implementation plan and theory of change (Annex 1) for RMEA. The following have been identified as *Key Success Factors* for Unitaid's interventions on RMEA:

- **Strategic product prioritization:** Unitaid efficiently and collaboratively assesses and prioritizes products for regionalization, ensuring a well-balanced and equitably distributed portfolio to meet specific regional healthcare needs.
- **Sustainable manufacturing:** Establishing commercially viable and sustainable manufacturing capacity for key product categories, enhancing self-reliance, promoting economic growth, and bolstering health resilience (including pandemic preparedness).
- **Improved access and affordability:** Increased access to quality assured essential health products. Regional manufacturing optimizes delivery costs and potentially leads to comparable or lower total landed costs, making products more affordable and enhancing accessibility for communities in need.
- **Environmental sustainability:** Increased sustainable manufacturing practices to minimize operational ecological footprint and lower logistics emissions through regionally produced health products.
- **Measurable impact on health outcomes:** Unitaid's targeted interventions improve health outcomes, showcasing their effectiveness in positively impacting communities and individuals across target LMICs.

RMEA alignment with PPPR and Climate & Health

The Secretariat is prioritizing the alignment of RMEA with other strategic areas. Integrating climate-related opportunities and risks into regional manufacturing interventions will contribute to making investments in this area more sustainable and competitive. Furthermore, adopting strong climate and nature standards and approaches from the start also offers opportunities to “leapfrog,” enabling acceleration, optimization, and efficiency of manufacturing essential health products in LMICs. Regional manufacturing also offers a platform to improve pandemic preparedness planning and response by ensuring the required capabilities for a more effective pandemic response are established or strengthened equitably across the target regions.
At the global level, there is consensus that a key lesson learnt during the COVID-19 pandemic is that access barriers (to both COVID-19 life-saving tools and, in general, to medicines and diagnostics to manage other persistent health issues in LMICs) were exacerbated due to supply chain vulnerabilities with the current geographical concentration of manufacturing capabilities. Transport disruptions, export bans, and border closures further compromised access to critical therapeutics for major diseases affecting LMICs when it was most needed. Pandemic preparedness efforts, hence, must also focus on expanding LMICs capabilities now to enable rapid access to pandemic products in the future. Sustainable and viable production in various regions should be supported that can address the needs for medicines and diagnostics supply in persistent major public health problems during the inter-crisis periods, while also remaining agile to pivot to surge demand for priority pandemic products as the need arises.

Regional manufacturing for climate smart health products

Unitaid's strategic emphasis and dual focus on promoting climate-smart health products and strengthening supply chain resilience through regional manufacturing initiatives create a compelling case for advancing synergistic collaboration and cooperative approaches. By aligning efforts in these areas, Unitaid aims to drive equitable access to health innovations while simultaneously ensuring environmental sustainability. By aligning efforts in these key areas, Unitaid can unlock dual benefits. For instance;

- By integrating climate-smart practices into health product manufacturing at the outset of regionalization projects, and ultimately leapfrogging, Unitaid can effectively work and invest towards advancing low carbon manufacturing methods and mitigate various environmental impacts throughout the product lifecycle.
- Regional onshoring of manufacturing not only enhances market proximity but also diminishes reliance on distant suppliers and centralized supply chains, thus reducing vulnerabilities to disruptions in global trade, or those linked to climate change-related crises and extreme weather events. By integrating climate-proofing measures like more resilient production infrastructures and diversified supply chains, regional manufacturing has the potential to bolster resilience of access to lifesaving products.

- Investment in climate-smart supply chains and technologies, coupled with regional manufacturing capabilities, facilitates adaptation to evolving environmental conditions and propels sustainable innovation in both product design, production processes and delivery models.

Unitaid acknowledges the potential economic, technological, and regulatory challenges associated with balancing climate-smart strategies with regional manufacturing initiatives. Leveraging its unique position and market shaping role within the global health architecture, however, Unitaid identifies a significant strategic opportunity to address these barriers cohesively and make well-informed tradeoff decisions. Through collaborative efforts, strategic partnerships, and holistic approaches, Unitaid aims to identify synergies and proactively mitigate tensions from the outset. Ultimately, Unitaid is committed to optimizing outcomes that prioritize equitable access to life-saving products while simultaneously promoting environmental sustainability. This comprehensive approach underscores Unitaid's dedication to driving positive change and nurturing sustainable solutions within the global health landscape.

4. Prioritization of intervention areas and development of business cases

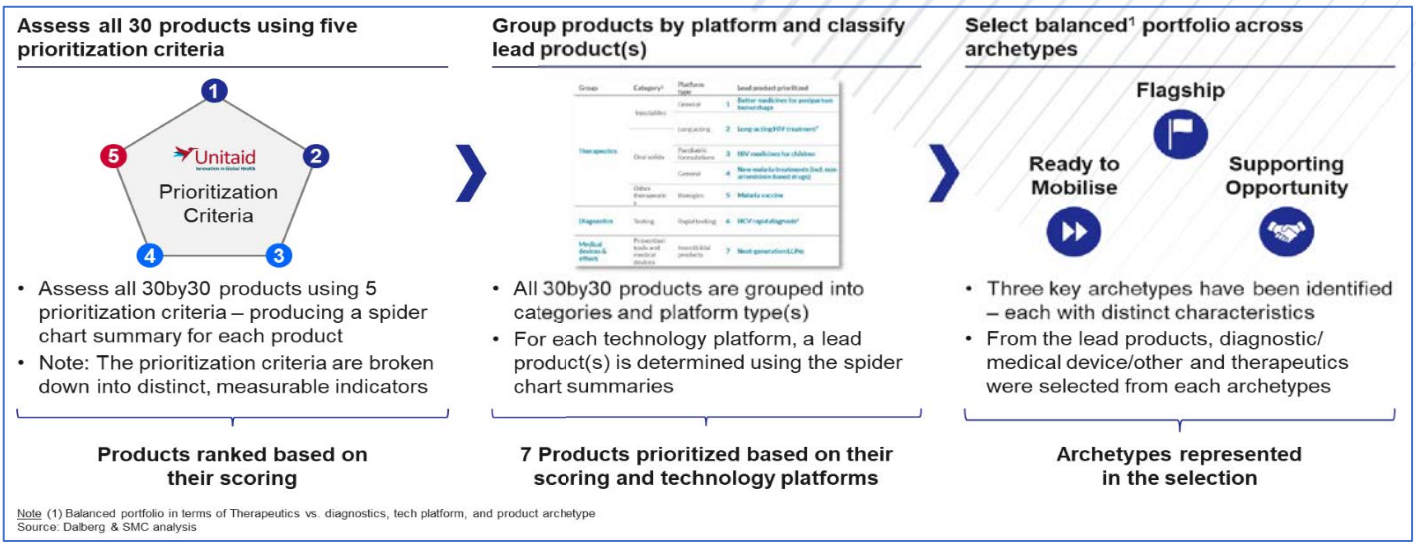
Prioritization of pathfinder products for unblocking ecosystem bottlenecks for regional manufacturing was conducted using a step-by-step multi-layered approach. The process was initiated by identifying five key criteria for assessing 30by30 product attributes, leveraging Unitaid's standard prioritization criteria. Products were prioritized based on:

a) **Resilience and equitable public health opportunity**
b) **Transformative potential of technology platform(s)**
c) **Historical investment and level of effort**
d) **Synergy with Unitaid's unique positioning**
e) **Product ecosystem and market readiness**

The 30by30 products portfolio was then subjected to these criteria and ranked as "high," "medium," and "low" priority across platform groups (Therapeutics, Diagnostics, or Medical Devices & Others). The technology platform to which high-priority products belonged was identified, and lead products for the represented technology platforms were selected. This approach ensures that manufacturing investments nurture both product-specific capacities and platform-wide ecosystems, taking into consideration platforms that could have broad application, including for pandemic response, such as parenterals.

Three distinct "archetypes" (Ready to Mobilize, Flagship, and Supporting Opportunity) that could form a well-balanced product manufacturing portfolio for Unitaid were then identified based on factors such as product development timelines and Unitaid's pathfinder role.

Figure 5: Graphic showing adaptation of Unitaid's prioritization methodology for use in product selection for RMEA



Ready to Mobilize products have nearer-term implementable solutions that unlock capacities, develop existing platforms, and/or capitalize on timely opportunities. These products allow Unitaid to play a lead role in nurturing regional manufacturing value chains. **Flagship Products** could be used to establish longer-term programs that will focus on foundational capacities and potentially establish novel product platforms. **Supporting Opportunities** comprise products where high impact potential is assessed, and Unitaid could play a supporting catalytic role due to the high engagement of other global health actors.

Figure 6: Output from the prioritization exercise

Priority	Therapeutics	Diagnostics	Medical Devices & Others
High Priority	• HIV treatment, including HIV medicines for children • **New malaria treatments, including non-artemisinin-based medicines** • **Better medicines for postpartum hemorrhage** • Long-acting PrEP and HIV treatment	• **Rapid diagnostic tests (HIV, HCV, including self-tests)** • Tools to detect preeclampsia/eclampsia • New tools to test main opportunistic infections [Diagnostics]	• Next-generation LLINs
Medium Priority	• Shorter and more effective TB preventative treatments, including long-acting formulations • Shorter/better regimen for DS-TB or DR-TB • Pediatric formulations for MDR-TB • Single-dose radical cure for P. vivax and accompanying diagnostics	• Point-of-care screen for other STIs [Diagnostics] • Single-dose radical cure for P. vivax and accompanying diagnostics • New point-of-care TB tests • True point-of-care HPV screening for cervical cancer, with HPV self-collection tools • Anemia diagnostics	• Innovations to increase access to oxygen therapy – see also: child survival* • New vector control tools, including ivermectin MDA, spatial repellents
Low Priority	• New treatments for neonatal sepsis [Therapeutics] • Point-of-care treat for other STIs [Therapeutics] • COVID-19 therapeutics, in particular oral antivirals for mild/ moderate cases	• New diagnostics and treatments for neonatal sepsis [Diagnostics] • Next-generation sequencing • Antigen rapid diagnostic tests • Medical imaging to diagnose TB (and other respiratory disease), including artificial intelligence enabled, mobile based, or point-of-care	• Cervical cancer treatment devices

** Unitaid has already initiated investment areas for regional manufacturing of Liquid Oxygen and innovative infant ventilator systems (bubble cPAP), as part of its flagship activities and leadership of the Global Oxygen Alliance, using specified funding (principally Canada, Japan) and based on EB approvals in 2023 and Q1 2024*

A deep dive was conducted for each of the prioritized product categories linked to an established Unitaid AFI, and a business case was developed using a representative product within the category. The business case focused on key product-specific issues such as market landscape, examining current manufacturing capacities that exist for the product/platform on the continent, as well as a potential market opportunity value chain, mapping each node of a product's value chain to determine what capacities exist on the continent, as well as associated gaps and barriers for scaled manufacturing. Business cases helped identify opportunities for Unitaid interventions to improve equitable access to these products, address barriers for scaled, cost-effective manufacturing, and strengthen the ecosystem elements to ensure sustainability and enhance pandemic preparedness. In a classical Unitaid approach, a bespoke differentiated intervention model will be deployed in each case based on the identified gaps and levels of maturity.

Engagement of key stakeholders

Stakeholder engagement has been a critical enabler in the evolution of Unitaid's RMEA initiative. The Secretariat adopted an iterative consultative approach to developing frameworks, strategies, and approaches that have shaped this initiative. At least 300 individuals across more than 130 organizations (including over 50 manufacturing companies) were engaged. Furthermore, the team facilitated and participated in multiple consultations with civil society and communities. Two of these consultations stand out as pivotal advocacy moments as well as a demonstration of Unitaid's thought leadership and convening role in this very important area of work: Unitaid's Industry Engagement Forum (October 2022), held in Cape Town, South Africa, and the G20 side event on "the development and manufacturing of diagnostics countermeasures," hosted by the Department of Pharmaceuticals, Government of India, FIND and Unitaid, with support from Market Access Africa (MAA) in April 2023. These convenings produced two valuable advocacy materials, an opinion paper and a meeting report, referenced multiple times by various stakeholders. The team also leveraged established field visits and manufacturer engagement mechanisms to meet over 30 manufacturers and visited 28 manufacturing sites across eight countries. The consultations also included meetings with officials from government institutions (including ministries of health, ministries of trade and industry, research institutions, and regulatory agencies), regional economic communities in Africa, AU agencies (Africa CDC, AfCFTA, and AUDA-NEPAD), AfDB/APTF, ASLM, USG agencies (USAID, PEPFAR), the European Commission, and PAHO.

In addition to gleaning from the knowledge and intelligence from the consultations and visits described above, the team working on the 30 x 2030 prioritization and business case development exercise conducted 29 focused interviews with key stakeholders, including partners (WHO, Global Fund, FIND, UNICEF, BMGF, Afrexim Bank, iPlus Solutions, CHAI), product developers and manufacturers.

5. Overview of proposed interventions

A combination of factors, including the recommendations of the prioritization exercise, existing portfolio opportunities, and funding landscape, has been used to establish a phased approach to Unitaid's regional manufacturing interventions. The first wave of interventions will focus on interventions that create pathways for a favorable ecosystem for regional manufacturing while using pathfinder products identified through the prioritization exercise to navigate and unblock ecosystem barriers. These pathfinder products will also strategically leverage the platforms provided by complementary supply and demand-side interventions being implemented by partners through our existing grant portfolio and otherwise and provide learnings for mainstreaming regional manufacturing initiatives into standard Unitaid access intervention design. **Wave one interventions include the establishment (or enhancement) of regional manufacturing capabilities for therapeutics and diagnostics for HIV and associated coinfections, improving access to expanded options for quality-assured malaria treatments to address emerging resistance to existing antimalarials, and better medicines for the prevention and treatment of postpartum hemorrhage.**

Figure 7: Overview of interventions

Focus area	Intervention	Linked AFI/Programmatic Priority (PP)	Products
HIV	**Quality assurance and portfolio expansion support** **Market Shaping advocacy with three major buyers**	*Improvement of Adult Anti-retroviral therapy in LMICs* UNITAID/EB22/2015/R4	*TLD (Adults) and Pediatric ALD*
PPH	**Generic formulation development & scale-up** **Quality assurance support**, focused on regulatory approval **Market shaping support**, offtake in public & private sectors **Market expansion**, through product licensing & tech transfer	*New tools for reducing maternal mortality* UNITAID/EB37/2020/R6	*Heat Stable Carbetocin* *Tranexamic acid* *Misoprostol*
Malaria	**Generic formulation development & scale-up** **Quality assurance support**, focused on regulatory approval **Market shaping support**, offtake in public & private sectors **Market expansion**, through product licensing & tech transfer	*Mitigating antimalarial drug resistance in high burden areas* UNITAID/EB41/2022/R1	*Dihydroartemisinin-Piperaquine (DHAP)* *Artesunate Pyronaridine (ASPY)*
Rapid Diagnostic Tests (RDTs)	**Portfolio analysis and business support** **Quality assurance support**, focused on regulatory approval **Product development and capacity expansion** support	*Optimizing management of coinfections and comorbidities in people living with HIV* UNITAID/EB27/2017/R5 **PP:** Drive HCV Elimination through Testing, Prevention	*HIVST* *HCV antibody or cAg (?)*
Cross-cutting	**Regional prioritization and capability mapping workshops; database development** **Clinical trials, BA/BE, and biologics research** capabilities upgrade **Capacity building and support to regional/continental institutions** **Build supply security,** via cost optimized API & other inputs **Capacity building for manufacturers by** shadowing	*Enable Access to monoclonal antibodies to treat and prevent infectious diseases in LMICs* *UNITAID/EB43/2023/11* ***PP:** Intellectual property, regulatory and innovative supply models (including regional manufacturing)*	*All*

In addition, to further build the resilience of the African manufacturing ecosystem and enhance on-continent capabilities for pandemic preparedness and response, wave one will also include interventions that expand the capacity and responsiveness of manufacturers to pandemics, including supporting capabilities to ensure adequate and expedited evaluation of products. Such capabilities would include clinical trial, bioavailability/bioequivalence and biologic research capacities that can bridge innovation, production and prompt market entry. Manufacturer capabilities for highly technical processes such as technology transfers will also be built through a shadowing program for manufacturers. Technologies developed and/or transferred in wave 1 will be leveraged for capacity building of additional manufacturers, and potential transfers to other underserved regions, especially the Latin America (LATAM) region. Interventions in wave 1 will also contribute to building the capacities of regional economic communities and regional and sub-regional technical, regulatory and coordinating entities.

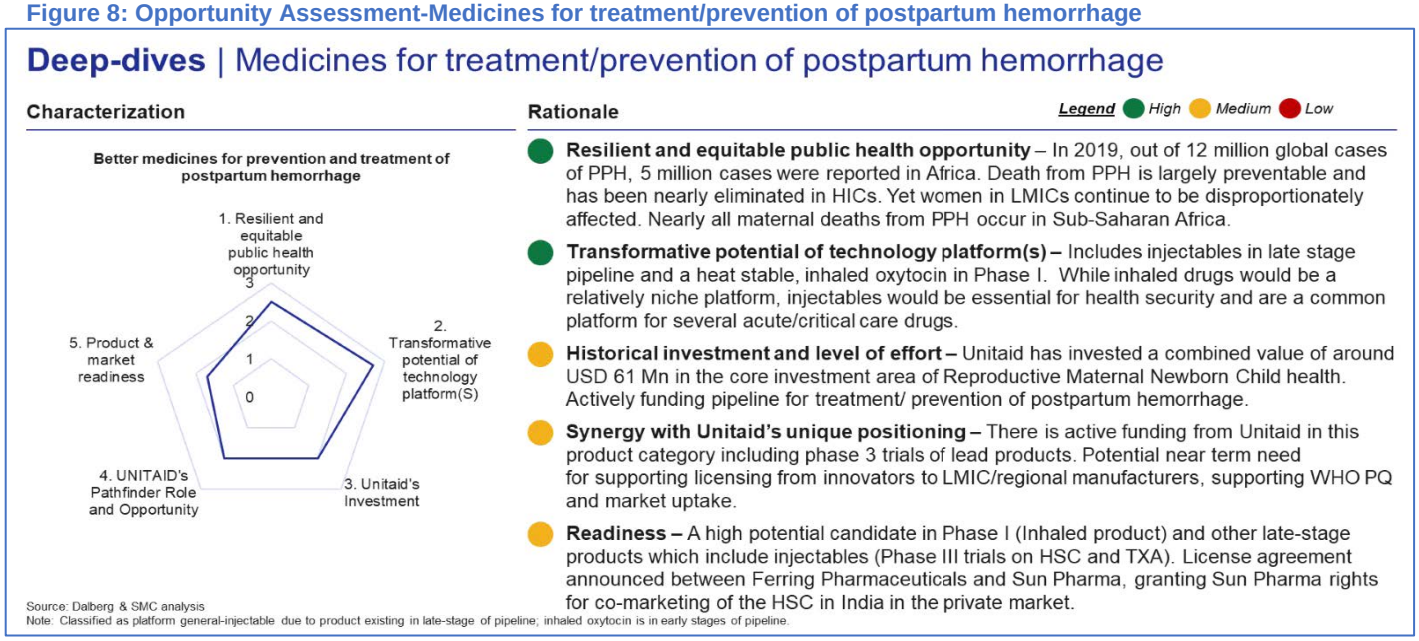
A second wave of investments would be initiated on the premise that wave one investments will have laid the foundation for more cross-cutting interventions that further enhance the robustness of the regional manufacturing ecosystem. Wave two interventions will entail investments in the LATAM region, additional product-specific interventions, and initiatives to build supply security and further optimize costs for established manufacturing capacity. These will include initiatives to develop and/or facilitate access to cost-optimized active pharmaceutical ingredients (APIs), the establishment of technology transfer hubs, and economics

assessments to further identify opportunities for cost-efficiencies/cost-competitiveness. Some of these initiatives, such as interventions on APIs and vertical integration/technology transfer hubs for diagnostics, are highly important and will be prioritized for resource mobilization efforts by the Secretariat.

5.1 Better Medicines for the Prevention and Treatment of Post-Partum Haemorrhage

To contribute to the Sustainable Development Goals for maternal health from 2015 to 2030, the Unitaid executive board endorsed a new area for intervention on **new tools for reducing maternal mortality** through resolution **UNITAID/EB37/2020/R6**. Postpartum hemorrhage (PPH) is the leading cause of maternal mortality worldwide. Each year, about 14 million women experience PPH, resulting in about 70,000 maternal deaths, with nearly all maternal deaths of PPH occurring in LMICs, primarily sub-Saharan Africa and South Asia (80% of all deaths)4. Heat-stable carbetocin (HSC), tranexamic acid (TXA), oxytocin, and misoprostol can help change the trajectory of PPH-related mortality. However, considerable market barriers exist in LMICs for existing formulations of three of these priority WHO-recommended drugs (HSC, TXA, misoprostol). There are opportunities with regional manufacturing of both existing and future formulations within the PPH portfolio.

Figure 8: Opportunity Assessment-Medicines for treatment/prevention of postpartum hemorrhage



Opportunities for Unitaid intervention in regional manufacturing

In addition to creating a favorable demand-side ecosystem through the active PPH portfolio, pivoting to manufacturing quality-assured HSC, misoprostol, and TXA on the African continent would be a critical strategic opportunity that could further enhance access in multiple ways. For example, Ferring's access price for HSC is not accessible in the private sector in LMICs, where approximately 60% of women seek care. Also, quality assured TXA and misoprostol are limited in many LMICs. Unitaid assessments have identified that some African manufacturers could manufacture these products at reasonable prices with the right mix of product development and market entry support. Furthermore, in the case of HSC, generic quality-assured products available to private sector markets would guarantee total market access and greater public health impact. However, the generic HSC market entry is currently impeded by intellectual property barriers for very few countries.

To support market entry of generic HSC, misoprostol, and TXA manufacturers, Unitaid could support formulation development and technology transfer to manufacturers with existing capabilities in Africa. In addition, Unitaid would further provide funding for regulatory approval support (through WHO PQ and/or AMRH/AMA) and catalytic market entry support using the PPH project portfolio and partners, such as UNFPA,

as a pathway to scaled uptake. For TXA and misoprostol, with an existing manufacturer in Africa, Unitaid could increase access to quality-assured products by providing support for regulatory approval for any identified existing or pipeline African manufacturers and further promote affordability and supply security by supporting market entry of an alternative supplier. These interventions will be associated with requisite contractual access commitments by the manufacturing partners. For HSC, however, access to generic products will be limited to countries without patent restrictions.

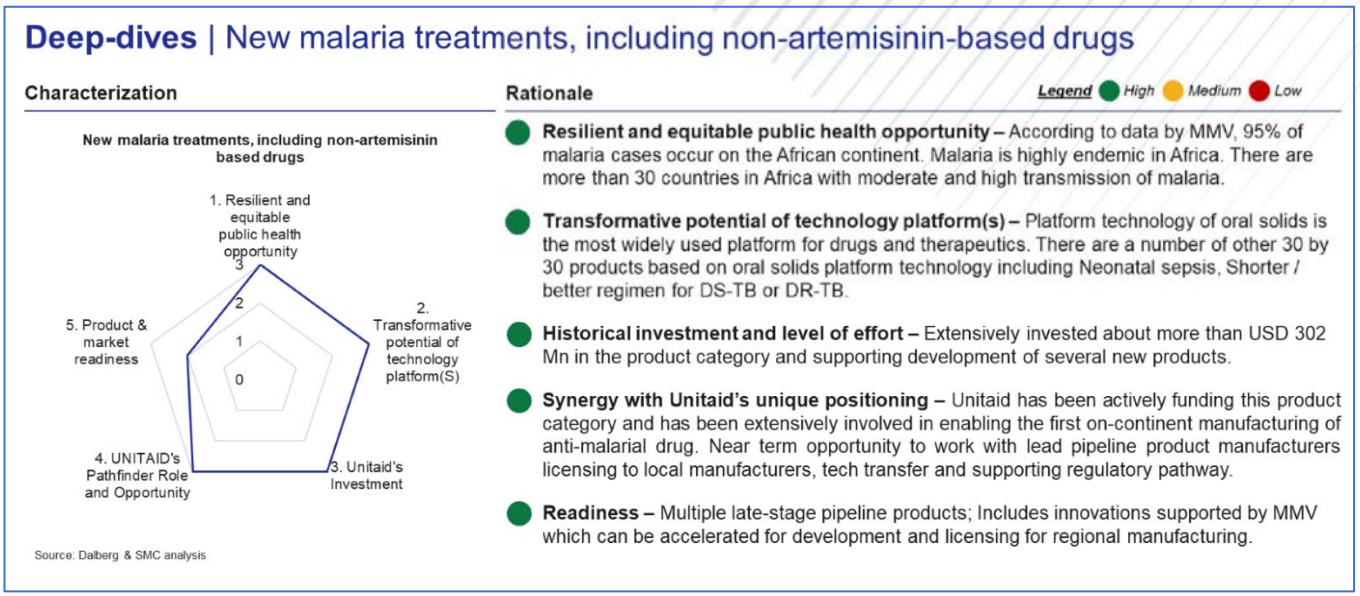
5.2 New Malaria Treatments, including non-Artemisinin-based drugs

In December 2022, the Unitaid Executive Board endorsed the area for intervention focusing on **mitigating antimalarial drug resistance in high-burden areas** through resolution **UNITAID/EB41/2022/R1** to contribute to the global malaria targets set out in the Global Technical Strategy for Malaria 2016—2030 and the Sustainable Development Goals. The global malaria burden persists, with progress plateauing in recent years. In 2023, there were 247 million malaria cases and 619,000 deaths5. Most cases occur in Africa (95%), and 77% of deaths affect children under five. Although malaria case incidence has reduced dramatically since 2000, from 2015, progress has plateaued, and as a result, the world is not on track to achieve global malaria targets. Access to quality malaria case management and treatment options remains a significant challenge in low-resource settings.

Antimalarial drug resistance in Africa is an urgent threat to the fight against malaria. The WHO recommends six ACTs that combine artemisinin-based compounds with a partner drug to treat malaria. Despite multiple ACT options, the market is dominated by a single ACT – Artemether Lumefantrine (AL), potentially driving resistance in Africa. Beyond the AL dominance, poor-quality medicines are another source of resistance to ACTs. Artemisinin partial resistance has been confirmed for the first time in Africa, specifically in Uganda, Rwanda, and Eritrea, though experts believe the problem is likely more widespread. Artemisinin partial resistance increases the risk of de novo emergence of partner drug resistance and, importantly, the spread of parasites that are less sensitive to the partner drugs, which can result in clinical treatment failures. Given the heavy reliance on ACTs in Africa, where most cases occur, the threat of drug resistance must be addressed urgently.

A near-term opportunity exists to limit antimalarial drug pressure by diversifying ACT markets through interventions that address supply barriers, generate demand for underutilized ACTs, and evaluate the impact and feasibility of strategies such as multiple first-line treatments (MFTs) to mitigate resistance. In light of challenges with older ACTs, e.g., tolerability due to side effects, partner drug resistance, and the fact that artesunate-amodiaquine (ASAQ) cannot be used as treatment in areas implementing seasonal malaria chemoprevention, diversification efforts will focus primarily on artesunate-pyronaridine (ASPY) and dihydroartemisinin-piperaquine (DHA-PPQ). Pipeline products, such as Ganaplacide plus lumefantrine will be kept on the Secretariat's close watch, with discussions initiated with the originators on appropriate mechanisms to integrate these into the Unitaid portfolio and by extension, the RMEA.

Figure 9: Opportunity Assessment-New malaria treatments, including non-artemisinin-based drugs



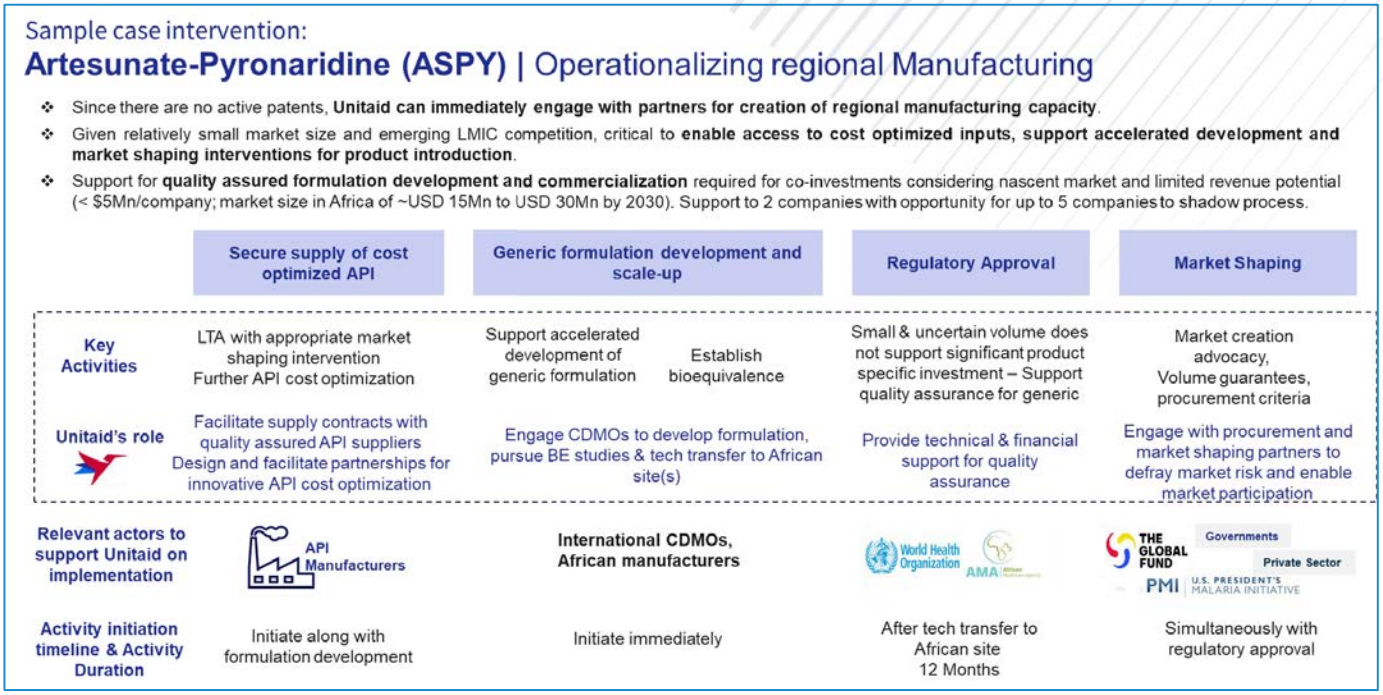
Oral solid dosage forms constitute one of the dominant pharmaceutical formulation types currently manufactured in Africa. Antimalarial medicines are a recurring feature on the import prohibition lists of malaria-endemic African countries with functional pharmaceutical manufacturing sectors. This is likely to increase significantly with the growing commitment of African countries to local/regional manufacturing. To ensure the imminent growth of the manufacturing of antimalarial medicines and align with the need for MFTs without compromising on any of the drivers of resistance, there is a need to ensure manufacturers in Africa produce affordable, quality-assured formulations of the first-line ACTs.

Opportunities for Unitaid intervention in regional manufacturing

The anti-malarial manufacturing value chain is already being nurtured in Africa. In collaboration with Unitaid, the Medicines for Malaria Venture (MMV) actively collaborated with local manufacturers for product development (sulfadoxine pyrimethamine (SP) with Emzor Pharmaceuticals in Nigeria) and support in regulatory review for WHO PQ (SP for Swipha in Nigeria and Universal Cooperation Limited-UCL in Kenya). Unitaid and MMV have continued to support African manufacturers in manufacturing quality-assured antimalarials. With Unitaid and MMV support, Emzor and Swipha have developed a quality-assured, child-friendly, dispersible formulation of SP. Swipha is expected to receive WHO pre-qualification for this product soon. UCL also received prequalification from the WHO for sulfadoxine pyrimethamine + amodiaquine (SPAQ) with support from MMV and Unitaid.

New API manufacturing capacities are emerging on the continent, with Mangalam having entered into a technology transfer agreement with Emzor Pharmaceuticals to support the production of five antimalarials: artemether, lumefantrine, dihydroartemisinin, sulfadoxine, and pyrimethamine. The API manufacturing facility is expected to start functioning in 2025 with an annual capacity of 400 metric tonnes.

Figure 10: Sample case intervention: operationalization of ASPY manufacturing in Africa



Building on the capabilities that currently exist on the continent, Unitaid should support viable African pharmaceutical manufacturers to nurture the manufacturing of cost-competitive, quality-assured ASPY and DHA-PPQ. Formulation development support would be key for African manufacturers through the creation of funded partnerships with contract development and manufacturing organizations (CDMOs) that could develop optimal formulations, conduct bioequivalence studies, and eventually transfer technology to African manufacturers.

This opportunity could also be leveraged to nurture CDMO capacity and build regional value chains on the continent through facilitating partnerships to establish/strengthen local CDMOs. Unitaid could further leverage the partnership with the WHO PQ department to support manufacturers for WHO prequalification. Unitaid should design market-shaping initiatives for accelerated market entry of the finished quality-assured products by leveraging learnings from the new AMDR projects and partnerships with the governments, the Global Fund, World Bank, and PMI.

The malaria portfolio offers the most promising opportunity on API cost-optimization. To secure an uninterrupted supply of cost-optimized API for identified African manufacturers, Unitaid could forge long-term supply contracts with WHO-prequalified API suppliers. In addition, Unitaid could lead the design and facilitate partnerships for innovative approaches for further cost optimization of APIs.

Regional manufacturing of quality-assured ACT also offers a chance to advance climate-smart product manufacturing. This entails integrating lower carbon API production routes to curtail carbon emissions (~78% of product emissions)[1], improving heat stability of ACTs – and potentially exploring use of semi-synthetic artemisinin as a critical alternative to natural artemisinin, which is susceptible to heat and drought during cultivation. The semi-synthetic Arteminisinin API is currently undergoing improvements in its development, intending to reduce the high fluctuating costs of the naturally derived Arteminisin API. Price optimization and adoption at scale of this semi-synthetic alternative could also significantly contribute to the affordability of the finished product.

[1] https://unitaid.org/assets/Report_From-milligrams-to-megatons_A-climate-and-nature-assessment-of-ten-key-health-products.pdf

5.3 Therapeutics and Diagnostics for HIV and related Co-infections

In support of Sustainable Development Goal 3.3 to end the AIDS epidemic by 2030, the Unitaid Executive Board in June 2017 endorsed an **area for intervention on optimizing management of coinfections and comorbidities in people living with HIV through resolution number UNITAID/EB27/2017/R5.** Within this AfI, the goal was to support access to health products for people with Advanced HIV Disease, people co-infected with Human Papilloma Virus (cervical cancer) as well as Hepatitis B and C, with a view to reducing AIDS-related mortality which had stagnated. Prior to this, interventions to increase access to optimal anti-retroviral therapy (ART), had been funded by Unitaid on executive board endorsement of the **AFI on improvement of Adult Anti-retroviral therapy in LMICs through resolution UNITAID/EB22/2015/R4.**

5.3.1 HIV Therapeutics

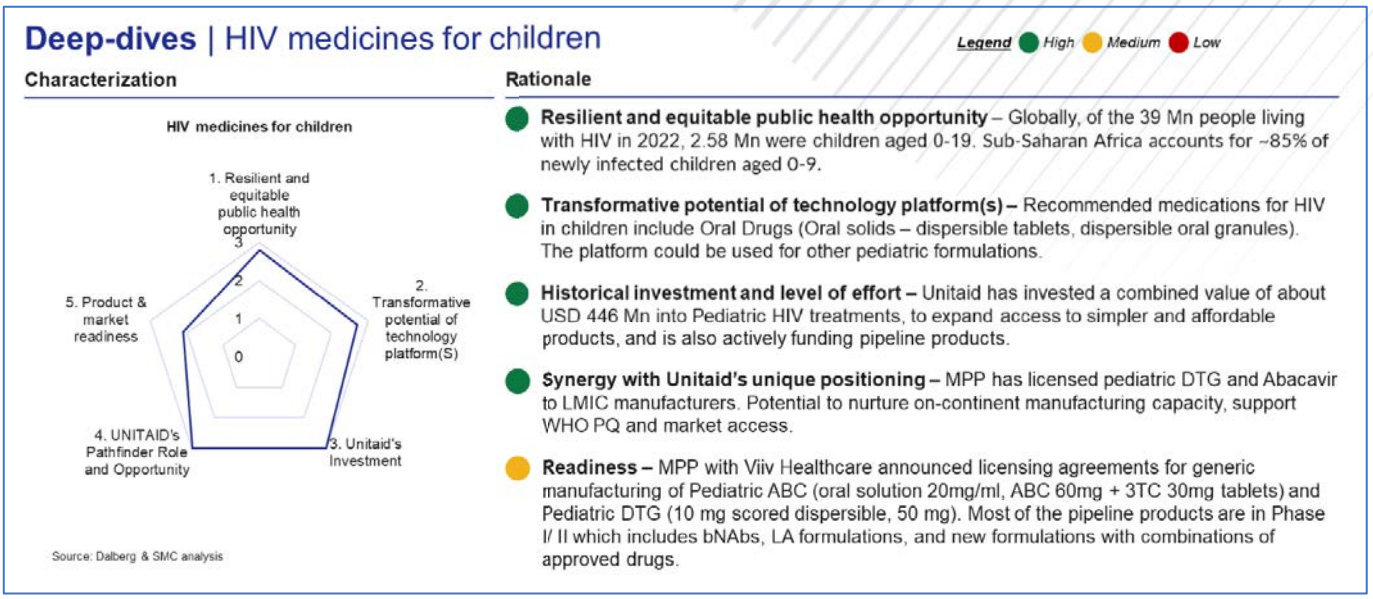
At the end of 2022, approximately 39 million people were living with HIV, with 66% of the global burden being in Africa (25.6 Mn people). In 2022, around 130,000 children aged 0-9 were newly infected with HIV, bringing the total number of children aged 0-9 living with HIV to 930,000. Nearly 85% of these children live in sub-Saharan Africa. Dolutegravir (DTG), developed by ViiV Healthcare, was USFDA approved in 2013. Since the WHO recommendation in 2019, DTG containing combinations with lamivudine and tenofovir (TLD) have replaced Efavirenz+Lamivudine+Tenofovir (TLE) as first-line treatment for adults and adolescents living with HIV, largely as a result of Unitaid supported partner interventions. For children living with HIV, a DTG-containing combination with abacavir and lamivudine (pALD) is the WHO-recommended first-line treatment for children under ten years and weighing less than 30kg.

Given its criticality for continuity of care and continental security, there is high strategic merit in nurturing the value chain for manufacturing TLD in Africa. For pALD, three Indian generic manufacturers (Cipla, Viatris, Aurobindo) have recently received US FDA approval for their fixed dose combinations, developed with Unitaid support. While the product is not a significant revenue driver for these large global generic companies due to the small pediatric market, Global Fund criteria for technical scoring deters current manufacturers from considering technology transfer to African manufacturers as portfolio breadth gives significant competitiveness in Global Fund tenders. **This has also incentivized an African manufacturer, Quality Chemicals Ltd., Uganda, to initiate development of pALD.**

The HIV drug market size in Africa in 2022 was estimated to be ~USD1.2 billion, with a penetration of ART of 86%. TLD constituted USD ~ 800 million (67% of the market by value, 86 % by volume) in 2022. Purchasing power is concentrated with three major procurers: the Global Fund (GF), the President's Emergency Plan for AIDS Relief (PEPFAR), and the South African Government, which engages in national tendering. Impetus from the major procurers has already triggered a focus on local manufacturing in Africa. However, the impact is likely to be limited due to key structural challenges. Actualizing sustainable engagement in regional manufacturing calls for further interventions. South Africa alone contributes to 32% of the HIV burden in Africa, while 38% of demand is concentrated in East Africa. With a TLD demand volume of 2.3 billion tablets in 2022, there is significant merit in nurturing manufacturing capacity in East Africa and already emerging capacity in South Africa.

Procurers' emphasis on local manufacturing significantly contributes to on-continent manufacturing capacity growth. The concentration of on-continent ARV manufacturing capacity in South Africa is attributed to the demand pulled by the South African Department of Health. In the 2020 tender, 66% of the volume was allocated to companies with local manufacturing capacity in South Africa; however, only about 10% of the total products supplied were manufactured locally.

Figure 11: Opportunity Assessment: HIV Medicines for children



PEPFAR has now laid down the explicit commitment to work alongside other partners and buyers to shift at least 2 million people on first-line ARV treatments to African-made products (which translates to annual demand volume of ~ 720 million tablets/~360 million tablets per supplier if serviced by two companies). In the most recent 3-year tender from the Global Fund, technical criteria (55% weight overall) included two (out of five) criteria that rewarded local manufacturing capacity. Global Fund, which historically procures only WHO PQ or FDA-approved antiretrovirals, has also signaled openness to accepting WHO-listed authorities' (WLA) approval. **While the demand-pull provides the impetus, structural challenges imply that additional interventions will be essential for the sustainable impact of regional manufacturing.** Despite the volume commitment provided by PEPFAR being a positive signal, it is an insignificant threshold to underwrite or incentivize investments in USFDA-approved manufacturing capacity (where the operating scale per unit for global peers benchmarked is ~2 to 5 billion tablets per year).

Opportunities for Unitaid intervention in regional manufacturing

To enable sustained competitiveness of regional manufacturers for generic formulations compared to the currently established global manufacturers, **Unitaid should lead data-driven advocacy for re-staging the procurement threshold for African-manufactured products to at least 30%.** Unitaid should also increase the likelihood of Global Fund's tender qualification for African manufacturers by supporting portfolio expansion for established African ARV manufacturers, especially those interested in producing pALD. Furthermore, Unitaid should support at least one (ideally 2) Southern African (preferably South African) manufacturer to achieve WHO prequalification and secure a DTG voluntary license from MPP, if required.
Data-driven advocacy for reasonable time-limited pricing premiums of not more than 10% to account for increased conversion costs and an acceptable and viable regulatory threshold for PEPFAR procurement of African manufactured products could also be a transformational intervention.

Figure 12: Summary of advocacy pitch for adjusting/setting the targets for ARV regional manufacturing

Local Manufacturing: Target threshold for local manufacturing

TLD offers opportunity to address key lacking element of scale in pharma manufacturing in Sub-Saharan Africa. To foster sustainable impact, threshold for local manufacturing target should ideally be reset to 30% or more of total volume procured by each major buyer:

- **Minimum scale to enable competitiveness for each manufacturer –** Global benchmarking points to minimum annual capacity of 1.5Bn tablets for competitive operations at standards compliant with WHO PQ. To underwrite baseline scale, TLD manufacturing should contribute to at least 33% of such a facility – implying volume per manufacturing facility of 495 Mn tablets (revenue potential of USD 69Mn)
- **Continental market volume** – Annual demand for TLD in Africa is estimated at 868Mn tablets in 2026, expanding to 1,019Mn tablets by 2030
- **Minimum target for local manufacturing** – Formulation manufacturing is likely to attract multiple companies (currently 10 to 14 competitors in GF & South Africa); Assuming 4 to 6 African companies nurture TLD supply capacity at scale with WHO PQ standards, to provide each of them minimum volume for sustainable scale, aggregate commitment to continental sourcing should be at least 2 Bn tablets or 30% of 2026 demand.

Fostering sustainable competitiveness: Minimum scale for each manufacturer			
Minimum scale for OSD facility to operate at WHO PQ level	Mn Tablets	1,500	
Target capacity utilization from TLD	%	25%	33%
Target annual production of TLD per facility	Mn Tablets	375	495
Target annual revenue from TLD at current prices	$ Mn	53	69

TLD Market in Africa		
Volume & Value	**2026**	**2030**
Annual TLD demand in Africa (Mn Tablets)	6,198	7,278
Market size at current prices	868	1,019

Local manufacturing commitment: Threshold for minimum economic scale						
Target procurement from on-continent manufacturers (as a % of total procurement for Africa)	%	10%	20%	25%	30%	40%
Aggregate TLD volume for on-continent manufacturing (based on 2026 demand)	Mn Tablets	728	1,456	1,820	2,184	2,911
Average volume per facility assuming 4 to 6 manufacturers on-continent supplying with WHO PQ	Mn Tablets	146	291	364	437	582

Similar to the malaria portfolio, a potential wave two intervention would be for Unitaid to support vertical integration of the ARV value chain through support to scale up existing laboratory scale API manufacturing in South Africa.

Decarbonization of TLD Manufacturing provides an opportunity within the climate and health – regional manufacturing nexus. While broadening the supplier base and reducing the time and distance from supply to market would yield climate resilience benefits, increasing regional production of HIV treatment in Africa offers a substantial opportunity to pioneer climate-smart manufacturing practices as “greenfield” initiatives from the outset of API manufacturing and drug formulation processes (>95% of the TLD treatment emissions). This approach would mark a significant milestone towards reducing carbon emissions linked with TLD-based drug formulations while addressing various other nature impacts (e.g., hazardous waste). Our M2M research findings indicate that the TLD treatment regimen could contribute to approximately 2.7 megatons of carbon emissions by the year 2030, assuming a projected demand for 30 million patients. Notably, the Dolutegravir component of this regimen exhibits a notably high carbon intensity, estimated at around 707 kilograms of CO_2 equivalent per kilogram of API[2]. Though not captured within the existing RMEA funding streams, the Secretariat will explore all available means to accelerate an intervention on this very important opportunity.

[2] https://unitaid.org/assets/Report_From-milligrams-to-megatons_A-climate-and-nature-assessment-of-ten-key-health-products.pdf

5.3.2 Rapid Diagnostic Tests

Fragile health systems in LMICs hinder testing, with significant diagnostic gaps, especially at the primary care level. The main drivers of inequitable access to diagnostics in LMICs include competition from High Income Country (HIC) buyers, delays due to slow regulatory approvals and lack of transparency in approval processes, fragmented and expensive supply chains, limited availability of well-performing tests for priority diseases in LMICs, and high dependence on a limited set of manufacturers. During the COVID-19 pandemic, this was demonstrated as the global demand for COVID-19 diagnostics significantly increased competition for available supplies, to the detriment of LMICs that had lower purchasing power.

Genetic and phenotypic variability is a major driver of the performance of diagnostics tools. Epidemiological differences across regions further complicate these and result in multiple implications, including mismatch of available tests and the needs in specific markets, as well as fragmentation of RDT markets such that there are significant unmet needs for tests in Africa and LATAM. Many global RDT producers are constrained to produce only large-volume products that can be supplied to multiple geographies to optimize supply chains. With shorter supply chains enabled by regional manufacturing, there is an opportunity to produce smaller quantities of tests if manufactured closer to the location of use. Paradoxically, the profitability and competitiveness of regional manufacturers of RDT need to be enhanced by ensuring such manufacturers have access to the markets for large-volume products such as HIV, malaria, pregnancy tests, and glucose tests.

Africa is one of the largest RDT markets, representing over US$1B, and is projected to double by 2030. Malaria RDTs account for almost half of the current market. However, only one African manufacturer has achieved WHO PQ status for an RDT. Unitaid's research and consultations indicate that RDTs' Cost of Goods in Africa can be as low as ~US$0.05/test; hence, manufacturing affordable, quality assured RDTs on the continent is feasible. Furthermore, existing differential pricing across countries by income classes makes access to diagnostic tests in the LATAM region challenging for specific niche tests (e.g., histoplasmosis tests and tests for screening STIs).

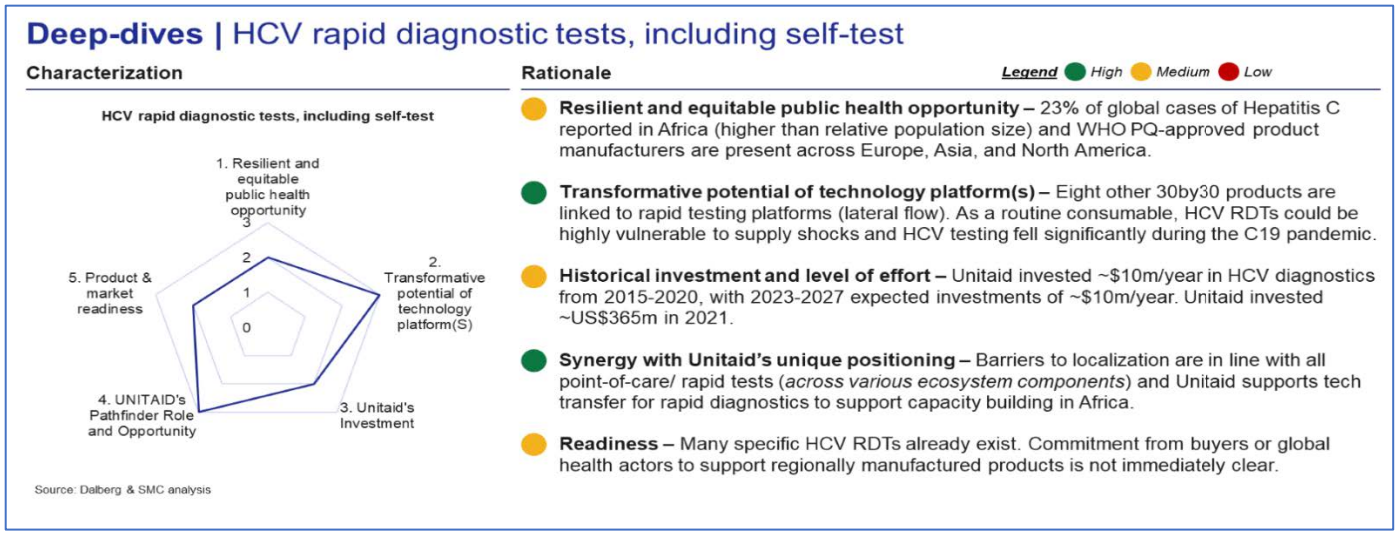
A major turning point in favor of manufacturing RDTs in Africa was in December 2022 when Ambassador Dr. John Nkengasong announced PEPFAR's commitment to African manufacturing and unveiled a commitment to procure at least 15 million HIV tests by African manufacturers by 2025. Since this announcement, Unitaid has maintained its position as a thought leader on access by supporting the mission through an existing collaboration platform with FIND. Unitaid and FIND have joined forces with PEPFAR, the Global Fund, and WHO to design interventions to help African manufacturers improve the cost and quality of their products and accelerate the pathway to market for quality assured RDTs. A special track for the GF/Unitaid/WHO expert review panel for diagnosticshttps://www.theglobalfund.org/en/news/2023/2023-08-08-global-fund-pepfar-unitaid-collaboration-accelerate-approval-african-manufactured-hiv-rapid-tests/ quality assurance (ERPD) for African manufacturers has been established. Also, to support capacity and capabilities upgrades, technology transfers, and quality assurance of RDTs, Unitaid, and FIND issued a request for proposals (RFP) to manufacturers of RDTs in Africa in October 2023.

Opportunities for Unitaid intervention in regional manufacturing

To enable sustained competitiveness of regional manufacturers for generic formulations compared to the currently established global manufacturers, Unitaid should build on the established work with FIND. Interventions with diagnostics manufacturers should focus on sustaining the growth of the diagnostics manufacturing sector, which is much less developed than that for pharmaceuticals. This is in alignment with Unitaid's regional manufacturing and PPPR objectives.
While HIV RDTs and self-test efforts advance as a priority, the Secretariat has scoped other areas to meet regional testing needs. Hepatitis C Rapid Diagnostic Tests (HCV RDTs), including self-tests, were identified through the prioritization exercise for potential investment, given their potential public health impact and market readiness. While there are few African manufacturers of Hepatitis C RDTs in the near term, there are opportunities for scaling up production. Most HCV RDTs are currently procured from external manufacturers, and the regional growth of manufacturing is hindered by barriers and the need for targeted policies. The HCV

core Antigen test development project, funded by Unitaid, also exposed the challenge of genotype variability as the test developed showed more promise with genotypes found predominantly in Africa but not those found in Asia. There is an opportunity to support HIV and malaria RDT manufacturers in the region in becoming competitive and including HCV/Hepatitis B RDTs as part of their portfolio in the medium term. Unitaid can be pivotal in addressing gaps and barriers, combining targeted and cross-cutting interventions. Additional opportunities to consider include the call for proposals on triple elimination, which will include RDTs for HIV and Syphilis, as well as work being done on screening for co-infections and co-morbidities of HIV within the Advanced HIV Disease portfolio are being considered.

Figure 13: Opportunity Assessment-HCV rapid diagnostic tests, including self-test



Interventions will include one or a combination of capacity and capabilities upgrades, technology transfers, and quality assurance of RDTs. Intervention should be anchored first on HIV professional or self-tests, which have a market commitment from scale-up partners, with conditionality that the supported manufacturer(s) should commit to developing and/or manufacturing HCV tests towards achieving the public health objectives.

Diversifying the market for RDTs production will not only enhance supply security but also foster the resilience of supply chains in the face of climate and nature hazards. Furthermore, exploring regional manufacturing of RDTs offers promising pathways to mitigate the detrimental climate and nature impacts associated with their lifecycle. It's important to note that RDTs contain single-use plastic and chemical ingredients, posing environmental risks from material processing and acquisition to production and disposal. Tackling these issues involves reducing the carbon footprint concentrated in upstream production (~90% of product lifecycle emission) and implementing measures to minimize environmental harm (e.g., water pollution) throughout the comprehensive product lifecycle.

6. Cross-cutting interventions

The following cross-cutting interventions have been prioritized for both regional manufacturing and PPPR:

a) **Regional prioritization workshops and capability mapping database development:** A regional approach to prioritizing focus products and interventions to strengthen regional value chains for health products is proposed. This will help ensure regions are manufacturing not only the things they can but also the things they need, and opportunities to collaborate across the regions are maximized. The continental institutions will coordinate the regional workshops. They will foster the actualization of viable regional value chains and ensure that interventions from Unitaid, governments, and other stakeholders are aligned and coordinated.

b) **Clinical trials, bioavailability (BA)/bioequivalence (BE), and biologics research capabilities mapping:** One of the debilitating gaps in the health products development and manufacturing ecosystem is the lack of cost-competitive facilities that can deliver current Good Clinical Practices (GCP) compliant clinical trials, including conducting bioequivalence studies and other relevant clinical research/bioanalytical operations which are key in the case of biologic products. To fill this gap, there is a need to better understand and map out the current landscape, identify opportunities for intervention, and design innovative ways to ensure that the ecosystem is adequately served cost-efficiently and that there is a bridge between regional capabilities for production and evaluation.

c) **Capacity building and support to RECs and regional and sub-regional technical, regulatory, and coordinating entities:** The success and sustainability of regional manufacturing initiatives hinge on the capabilities of national, regional, and continental institutions. The initiative will design capacity-strengthening opportunities in its operations either directly or by leveraging Unitaid's existing partnerships, such as the collaboration with WHO RPQ.

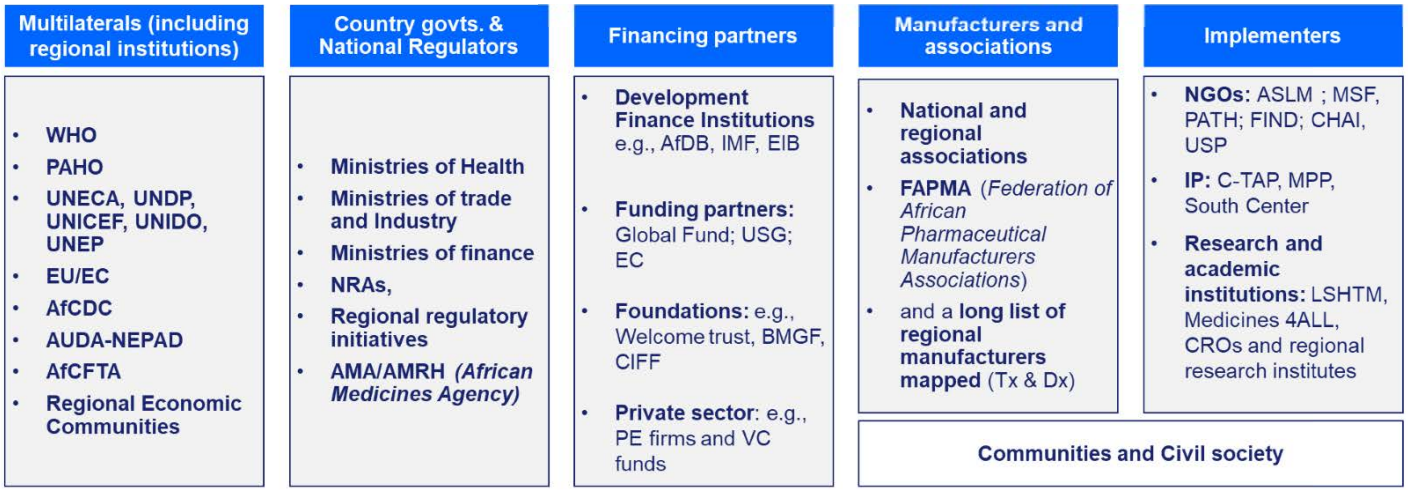
d) **Build supply security, via cost optimized API & other inputs (market shaping for key manufacturing inputs:** Improving the quality and reducing the costs of key manufacturing inputs, starting with Active Pharmaceutical Ingredients (APIs) and prioritized excipients, is a pivotal lever for enhancing regional pharmaceutical manufacturing in Africa. By improving the quality of these essential components, pharmaceutical companies can ensure the production of safe, effective, and reliable medicines. This bolsters confidence in local pharmaceutical products and aligns with international quality standards, opening opportunities for export markets. Moreover, cost reduction in APIs and excipients directly impacts the affordability of medications, making them more accessible to a wider population within the region. This intervention will also focus on ensuring greener manufacturing practices are adopted by regional manufacturers.

e) **Capacity building for manufacturers by 'shadowing':** Many stakeholders, especially the manufacturers, have listed human capacity development as one of the top challenges hindering the growth of the health products manufacturing value chain. While funding didactic training may be out of the scope of this initiative, Unitaid will design an innovative capacity-building program that creates an opportunity for one or two additional manufacturers (or staff of research institutions) to understudy any product development or technology transfer process funded by Unitaid. In addition, any intellectual property (or know-how) developed during implementation will be made public goods by direct sharing or licensing through the MPP mechanism.

7. Strategic partnerships for regional manufacturing

Strategic partnerships double as a Unitaid strategic objective and an important element of the RMEA initiative. Over the past 18 months, Unitaid's influencer role has consistently progressed within the global health regional manufacturing community. Unitaid will leverage this strengthened position to ensure high effectiveness and efficiency in executing the initiative.

Figure 8: Stakeholder mapping for the regional manufacturing initiative



Unitaid's existing **technical partnerships** with the WHO division on Access to Medicines and Health Products, the Global Fund, PEPFAR, FIND, CIFF, and MPP are notable levers to support effective delivery. **Governments, regional institutions, civil society, and communities** help steer the design and implementation of interventions and are at the core of Unitaid's mission. Unitaid's relationship with **donor governments, foundations, development finance institutions, and other funding partners** is three-pronged: first, to serve as a thought partner and pathfinder, offering Unitaid's years of experience and thought leadership; secondly, Unitaid will continue to explore opportunities to co-finance interventions, to make maximum use of Unitaid investments; and finally, Unitaid will continue to engage in mobilizing additional resources to support the initiative.

8. Potential impact

Successful implementation of identified interventions within Unitaid's regional manufacturing initiative would have significant public health and economic impact, broadly translating to progress towards achieving global health targets for the key morbidities addressed. Establishing sustainable manufacturing capacity for key product categories would enhance self-reliance, promote economic growth, and bolster health resilience (including pandemic preparedness) for the targeted regions. In addition, increased access to quality-assured essential health products would be achieved as local manufacturing reduces costs, making products more affordable and accessible to communities in need. Using regional manufacturing to introduce greener manufacturing technology would minimize operational ecological footprint and lower logistical emissions through regionally produced health products. Potential key drivers of impact are:

- Improved access: either due to reduced product delivery timelines or prioritized access
- Lower cost: because of reduced shipment distance
- Enhanced quality: improved capacity of regional production can promote quality assurance
- Increased economic value: local production creates jobs - a source of income and economic development
- Reduced risk of supply disruption due to natural disasters, cyberattacks, or global epidemics affecting the point of production

Estimates for each product's potential impact will be developed separately. Regional manufacturing of some products may come at an added cost, but this is outweighed by the need for supply security.

9. Risk

The strategic risks associated with these opportunities are low, given the high priority of regional manufacturing on the agenda of key global health stakeholders and the alignment of the product selection with epidemiological patterns and market needs in the selected regions. The proposed investments align with Unitaid's areas of strength, build on existing initiatives, and complement other implementation efforts within Unitaid funded projects, reinforcing Unitaid's strategic positioning and increasing the likely impact of the interventions.

The landscape for these opportunities is marked by potential partners and a supportive ecosystem, coupled with opportunities to forge ground-breaking partnerships with entities like development finance institutions and regional coordination mechanisms. However, the navigation of complex multiple regional coordination mechanisms to unblock ecosystem barriers for creation regional value chains in Africa presents a risk for effective and timely implementation. Unitaid aims to mitigate this through the creation of sub-regional value chains for pathfinder products as proof of concept for broader continental adoption.

The sustained success and market presence of regional manufacturers fundamentally depends on securing sustainable markets for their products and establishment of effective procurement strategies. Without clear commitments from global procurement entities and Ministries of Health to procure these essential products, the ability to scale and extend the impact of these investments could be at risk. This emphasizes the importance of a proactive approach in determining viable business models appropriate for the setting, establishing robust partnerships and gaining the required support and purchase price/volume commitments for sustainability.