

End of Project Evaluation for Unitaids Investment in Enabling TB Preventive Treatment in High-Risk Populations

Unitaid

24 July 2026



FINAL REPORT

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ACRONYMS

Acronym	Definition
1HP	One-month daily isoniazid and rifapentine regimen for TB preventive treatment
3HP	Three-month once-weekly isoniazid and rifapentine regimen for TB preventive treatment
3HR	Three-month daily isoniazid and rifampicin regimen for TB preventive treatment
API	Active pharmaceutical ingredient
CBO	Community-based organisation
CCSE	Civil society and community engagement
CHAI	Clinton Health Access Initiative
CHIP-TB	Child household contact investigation and TPT delivery study under I4TB
CLHIV	Children living with HIV
COP	Country Operational Plan
CSO	Civil society organisation
DOLPHIN	DOLPHIN studies on dolutegravir and rifapentine-based TB preventive treatment
DR-TB	Drug-resistant tuberculosis
DTG	Dolutegravir
EMAV	Early Market Access Vehicle
FDC	Fixed-dose combination
GDF	Global Drug Facility
HHC	Household contact
I4TB	IMPAACT4TB
IPT	Isoniazid preventive therapy
KNCV	KNCV Tuberculosis Foundation
LONGEVITY	Unitaid-funded project on long-acting formulations for TB preventive therapy
MDR-TB	Multidrug-resistant tuberculosis
MPP	Medicines Patent Pool
NTP	National Tuberculosis Programme
PEPFAR	United States President's Emergency Plan for AIDS Relief
PLHIV	People living with HIV
RPT	Rifapentine
TAG	Treatment Action Group
TB-CHAMP	TB Child and Adolescent Multidrug-Resistant Preventive Therapy trial
TPT	Tuberculosis preventive treatment
WHO	World Health Organization

EXECUTIVE SUMMARY

Introduction

Tuberculosis (TB) remains the world's leading infectious killer. Worldwide, one in four are infected with TB bacteria, however only 5-10% will go on to develop active TB disease. Preventing this progression is a cornerstone of the World Health Organization (WHO) Global End TB Strategy (2015-2035) and WHO recommends TB Preventive Treatment (TPT) for those most at risk: People living with HIV/AIDS (PLHIV), household contacts of people with active TB disease, and other high-risk groups, supported by effective screening, early diagnosis, and prompt treatment.

For decades, TPT uptake remained limited because existing regimens were long (6–36 months), making them impractical to deliver in resource-constrained settings where TB burden is highest. A major advance came in 2018 when WHO recommended shorter rifapentine-based regimens (3HP and 1HP¹). However, country and donor adoption lagged due to unresolved questions about use with dolutegravir among PLHIV, the high cost of rifapentine (US\$72) from a single supplier (Sanofi) with insufficient production capacity in relation to global need, and uncertainty about implementing the new regimens within weaker health systems. The absence of a fixed-dose combination (FDC) for 3HP and 1HP also meant an increased pill burden, raising concerns about acceptability and treatment completion. For children, the lack of a child-friendly 3HP formulation and dosing guidance for the youngest age groups further constrained access.

The IMPAACT4TB project

To address these challenges, Unitaid launched the 'Increasing Market and Public Health Outcomes through Scaling Up Affordable Access Models of Short Course Preventive Therapy for TB (IMPAACT4TB) (I4TB) project in 2017, led by the Aurum Institute (Table 1). Following the original project, additional resources were added in 2022 to address priority TPT access barriers for children and pregnant women.

The flagship I4TB project formed part of Unitaid's broader TB prevention portfolio, which comprised multiple complementary investments targeting different population groups and both drug-sensitive (DS) and drug-resistant (DR) TB. The portfolio also included several cross-cutting enabling investments, such as support to the WHO Global TB Programme and WHO Prequalification, aimed at accelerating the adoption of new TB drugs and formulations and strengthening normative guidance.

Table 1: Unitaid IMPAACT4TB overview

Goal: To reduce TB incidence and deaths among PLHIV and child contacts through sustainable implementation of affordable, quality-assured 3HP			
Outcomes: Increase the number of PLHIV (15-49) and child contacts <5 years starting treatment with affordable, quality-assured 3HP; and contribute to revising WHO preventive therapy guidelines based on evidence generated.			
Grantees: Aurum Institute (lead), Implemented with CHAI, KNCV, Johns Hopkins University (JHU), Treatment Action Group (TAG)			
Duration	Budget	Key objectives	Focus countries
Original grant 2017-2022	US\$ 58.9m	To catalyse access to short-course TPT for PLHIV and child contacts by removing critical market and access barriers and creating the conditions for sustainable scale-up	12 high burden countries: Brazil, Cambodia, Ethiopia, Ghana, India, Indonesia, Kenya, Malawi, Mozambique, South Africa, Tanzania, and Zimbabwe
Extension 2022-2025	US\$ 19.1m	To increase the number of child and adult household contacts (HHCs) and PLHIV started on TPT and contribute to the revision of WHO guidance for children and pregnant women	
Total project period: 8 years, 4 months (Total value of US\$ 78.0m)			

¹ 3HP and 1HP combine rifapentine and isoniazid, taken once weekly for 3 months (3HP) or daily for one month (1HP) to kill latent TB infection. Source: IMPAACT4TB Clinical Guidelines.

Evaluation objectives, framework and methodology

This end-of-project evaluation assesses the extent I4TB and Unitaids' complementary TB prevention investments accelerated access to quality-assured, affordable rifampentine-based TPT for high-risk groups, with a focus on effectiveness, scalability, impact, and sustainability. It also examines the contribution of Unitaids through its roles as a pathfinder, investor, and influencer. As a learning-focused evaluation, it explores key lessons on community and civil society engagement (CCSE) and market shaping. While centred on I4TB, the evaluation also considers other Unitaids TB prevention investments to assess coherence and contributions to portfolio-level results. Figure 1 summarises the evaluation methods and data sources. A key limitation was the considerable time elapsed since the original I4TB grant in terms of stakeholder recall and availability, with further detail and mitigations in the full report.

Figure 1: Evaluation methods and data sources

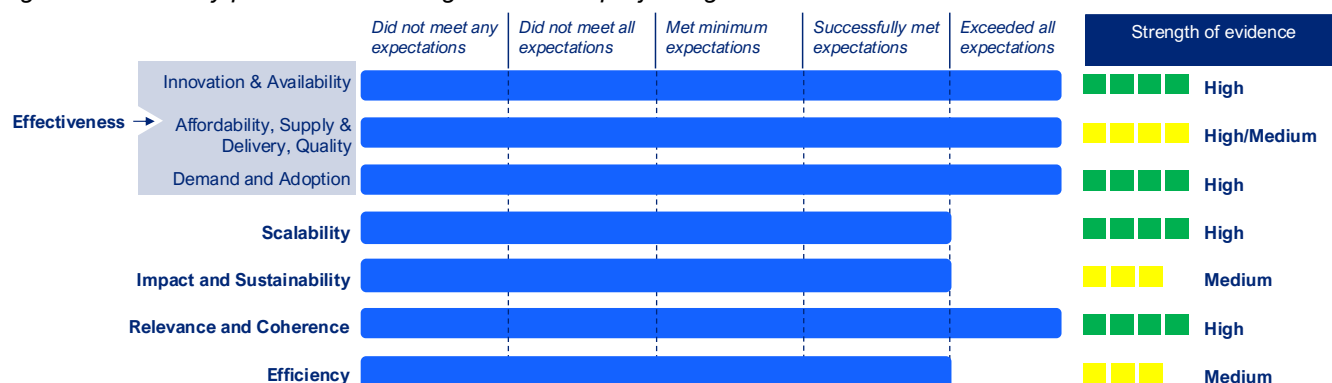


Summary of project performance and Unitaids' contribution

Figure 2 provides an overall summary of project performance across the Organisation for Economic Co-operation and Development - Development Assistance Committee (OECD DAC) evaluation criteria, and strength of evidence.

I4TB was a highly successful Unitaids investment. The project exceeded expectations in addressing priority access barriers to rifampentine-based TPT and in its relevance and coherence, while meeting expectations across the remaining evaluation criteria. It made a substantial contribution to global adoption of short-course TPT, with more than 100 countries procuring rifampentine-based TPT by 2025, and shorter regimens accounting for almost half of all TPT initiations globally. While TPT scale continues beyond the close of I4TB country activities in 2022, countries are not on track to reach the ambitious global target of 90% coverage by 2027 among high-risk populations. In 2024, TPT coverage reached 58% among PLHIV and 25% among household contacts—well below the target but representing substantial progress from baseline levels of less than 40% and less than 5%, respectively.

Figure 2: Summary performance rating of the I4TB project against OECD DAC evaluation criteria



The evaluation finds that alongside its investor role, Unitaid played a particularly strong pathfinder and influencer role in I4TB. Key contributions included shaping the project to address critical evidence gaps important for global 3HP demand, supporting studies on 3HP use among pregnant women and young children, championing a 3HP fixed-dose combination (FDC) and child-friendly formulations, and engaging with PEPFAR, manufacturers, and other stakeholders to accelerate policy adoption and market development. Examples of Unitaid's *direct contribution* to key I4TB achievements are summarised in Figure 3.

Figure 3: Unitaid contribution assessment

Role	I4TB key achievement	Assessment of Unitaid contribution			Strength of evidence
		Low	Medium	High	
 Pathfinder	- Foundational DOLPHIN studies demonstrating safety of 3HP for PLHIV on dolutegravir, supporting market confidence in 3HP demand - Closed evidence gaps for groups often neglected in clinical and operational research (children and pregnant women). - Stimulation of generic 3HP and 1HP, including FDC	[Full bar to High]			High
		[Full bar to High]			High
		[Full bar to High]			High
 Investor	- Absorbed early market shaping risks for Sanofi and generic rifapentine formulations - EMAV for paediatric-friendly rifapentine, securing same price as adult formulation, and cheaper vs. alternatives - Global public goods: clinical and operational evidence in different epidemic and health systems contexts - Scale of 3HP for PLHIV and child and household contacts	[Full bar to High]			High
		[Full bar to High]			High
		[Full bar to High]			High
		[Full bar to High]			High
 Influencer	- Key brokering role with PEPFAR and partners to agree to US\$15 for Sanofi rifapentine product - Global TPP for adult 3HP FDC - PADO engagement to agree on a paediatric dispersible 150mg rifapentine in place of an FDC - Coordination with WHO, PEPFAR, the Global Fund, manufacturers, civil society and country stakeholders, helping shape discussions around TPT access, evidence priorities, pricing and implementation approaches.	[Full bar to High]			Medium
		[Full bar to High]			Medium
		[Full bar to High]			Medium
		[Full bar to High]			High

Evaluation key findings

The main evaluation report contains 15 findings, along with two learning briefs: on CCSE and market shaping, analysis of what worked well and less well across the project components and their implications for future Unitaid investment. The evaluation findings and insights are summarised into the 5 key finding areas below.

Key finding area 1: I4TB catalysed a 70% reduction in the price of 3HP, market entry of quality-assured FDC products and a child-friendly formulation, and strengthened supply resilience through market diversification. This was the combined result of direct Unitaid engagement, I4TB consortium efforts, and a well-coordinated effort amongst key partners.

Unitaid market shaping achieved the first agreement with Sanofi to lower the price of 3HP from US\$72 to US\$15 per adult course. Unitaid's added value was described as its ability to convene and coordinate actors including Sanofi, PEPFAR, the Global Fund, iPlus solutions, CHAI, MedAccess and PAHO early on, and flexibility to apply the most appropriate market shaping instruments at different timepoints and for different products. Clarity from PEPFAR on a target price was a key breakthrough, with Unitaid taking on early market risks through its adjustable purchase order with Sanofi and targeted market shaping support to generics entering the market. This was later complemented by a Volume Guarantee (VG) by MedAccess to support multi-year market stability. The price of 3HP has since further declined to under US\$10 through the VG and subsequent market shaping efforts. Later in 2024, Unitaid and I4TB also implemented an Early Market Access Vehicle (EMAV) to encourage demand for a paediatric-friendly rifapentine. This 150mg dispersible formulation developed by Lupin and WHO Prequalified in 2024 is

considered a “game-changer” for children at risk of TB disease, and the EMAV a valuable ‘demand-driven’ market shaping tool for new product introduction.

“From the \$72 per patient cost down to \$15 was one of the reasons that the government eventually came to agree that we can move to shorter regimens.” (Tanzania stakeholder)

Early on, 3HP demand significantly outstripped available supply, which was also challenged by impurity concerns, leading to rationing. Use of the ‘ARV procurement working group’ to coordinate 3HP procurement became a best practice model for procurement coordination, offering good insights on managing the demand and supply interface in a multi-donor, multi-stakeholder context.

Key Finding Area 2: Evidence generation was fundamental to policy change and scale-up, most significantly for introducing 3HP within HIV services, which was a key scale platform.

Evidence generated through I4TB was highly influential in shaping global and national policy. In total approximately nine WHO policies and guidelines were significantly, or in-part, informed by work under I4TB to date, including the foundational WHO TPT 2018 and 2020 guideline expansion for 3HP on PLHIV taking dolutegravir, as well as the WHO TPT 2024 guidelines on pediatric dosing, and the 2025 HIV treatment guidelines. Together with negotiations with PEPFAR on 3HP affordability, the DOLPHIN study evidence which informed the 2018 TPT guidelines was a key enabler of market confidence. All 12 I4TB countries updated their TPT policies during the project period and as of 2025, more than 100 countries are procuring 3HP.

“These studies were the key ones informing policies...and government decisions. And the WHO endorsement was key.” (Global stakeholder) *“The Aurum-led consortium has been the go-to group for accessing evidence on TPT.”* (Global stakeholder)

Unitaid’s WHO enabler grant was highly complementary to I4TB, with WHO playing a central role in advancing rifapentine-based TPT. In particular, WHO played an important role in ensuring I4TB research questions and design aligned to key policy priorities. The WHO guidelines for TPT were updated multiple times over 2018 to 2024, utilizing the results of Unitaid-supported research, with WHO coordinating regularly with National TB Programs to accelerate their adoption. WHO enabler support included the development and publication of ‘Guidance on evidence generation for new regimens for TPT’², which consolidated lessons learned from the research supported by I4TB and other TPT trials.

The 2022 project extension had a significant focus on closing evidence gaps for pregnant women and children living with HIV (DOLPHIN-Moms and DOLPHIN-Kids). These studies, together with the EMAV for a dispersible rifapentine, reinforced Unitaid’s leadership in ensuring these groups are not left behind. The project also generated practical implementation evidence to guide decision-making on optimal delivery models and choice of 3HP vs 1HP regimens in different contexts.

Key Finding Area 3: Community engagement was essential to successful product introduction, particularly where communities and health providers were ‘starting from a deficit’.

A distinctive feature of I4TB was the strong integration of CCSE. Civil society organisations played a critical role in building treatment literacy, addressing misconceptions about TPT, supporting demand generation, and maintaining confidence during supply disruptions and product quality concerns. Stakeholders consistently reported that TPT introduction required rebuilding confidence among providers and communities following decades of experience with longer regimens where acceptance for 3HP was ‘starting from a deficit’

“The impacts of [I4TB] cannot be underestimated. It has shaped and made possible the very rapid uptake of 3HP. And nowadays, if you come to [these] countries, people talk about 3HP as if it’s just

² WHO (2025). Guidance on evidence generation on new regimens for tuberculosis preventive treatment. Available at: <https://tbksp.who.int/en/node/3187>

normal. As if it's nothing special, which is, of course, good but then you forget it's only been a few years.” (I4TB implementing partner)

Despite the overall effectiveness of CCSE, the scale and duration of funding allocated underestimated the level of effort required to sustain community engagement and policy influence. The small grants programme represented less than 1% of the total I4TB budget. While widely regarded as catalytic, the one-year funding cycle limited sustainability, continuity of advocacy efforts, and long-term relationship building with policymakers and communities offering important lessons for future CCSE. Since the close of I4TB, TB civil society partners have also been significantly affected by the dismantling of USAID in 2025 which had been the largest bilateral TB funder, further undermining sustained community engagement in TB.

Key Finding Area 4: I4TB catalysed uptake of 3HP for PLHIV and child contacts. It was less successful in adoption of TPT for adult household contacts due to lower prioritisation at the policy level. The project made a significant contribution to the country and global scale-up of rifampentine-based TPT.

By the end of 2022, more than 504,000 PLHIV and nearly 45,000 household contacts had initiated TPT through I4TB-supported and catalytic scale-up driven by governments and other partners across the 12 project countries. Uptake was supported by strong CCSE and I4TB's deliberate integration of 3HP into existing structures and systems, including data systems, which strengthened country ownership and implementation.

I4TB also contributed to substantial global scale-up. WHO reports the share of TPT initiations using shorter regimens (including 1HP and 3HP) increased from less than 1% in 2018 to 44% in 2024. This represents a growth from 0.19 million people in 52 countries in 2021, to 2.1 million people in 88 countries in 2024.

The evaluation examined trends in 3HP coverage after I4TB country activities ended in 2022. Coverage among PLHIV has levelled off since its 2020 peak, reaching 58% in 2024, suggesting that earlier intensive enrolment efforts were not sustained. Initiations among household contacts are increasing, reaching 25% in 2024, but the gap remains substantial. Overall, global TPT coverage has progressed, but not at the pace needed to reach the 2023 UN High-Level Meeting target of 90% coverage among high-risk populations.

“The need might be there, but the demand is not there...because programs aren't doing contact tracing.” (Global Stakeholder)

Many of the barriers that constrained early TPT scale-up have now been addressed at global and country level. The principal constraints to future growth increasingly relate to service delivery, particularly household contact investigation which is under-funded (USAID was previously a key funder), screening, diagnosis, provider confidence, and linkage to care, along with financing.

Key Finding Area 5: Unitaïd demonstrated agility in seizing opportunities to advance the 3HP agenda and employed a flexible approach to respond to emerging evidence and implementation experience. Together with Aurum's strong leadership and consortium partners, this contributed to the project's overall effectiveness.

Throughout I4TB, Unitaïd adapted its approach in response to evolving market conditions, implementation challenges, and emerging evidence. Examples included incorporating the DOLPHIN studies during grant development to address a critical evidence gap for PLHIV on dolutegravir, which were implemented relatively swiftly in existing Aurum research sites; strategically expanding the US TBTC Study 35 to include additional African-based sites to address an important evidence gap on 3HP dosing for children under 2 years; tailoring market-shaping approaches and instruments as the rifampentine market evolved; reallocating resources to address supply disruptions and nitrosamine-related challenges; supporting procurement and scale-up in additional countries beyond the original project scope; and extending the project to address priority access barriers for children and pregnant women (DOLPHIN-Moms and DOLPHIN-Kids studies). Stakeholders consistently viewed this flexibility as a key strength, enabling Unitaïd and its partners to maximise opportunities for impact, rapidly address emerging barriers, and maintain momentum towards global adoption of rifampentine-based TPT. Aurum, based in South Africa, was a

strong lead partner and stakeholders consider the full consortium was well designed and leveraged its expertise and networks.

Recommendations for Unitaid

Recommendations are provided on: (i) Unitaid's investments in TPT; and (ii) broader recommendations for Unitaid's grant-making approach across its portfolio, in support of its roles as a pathfinder, investor and influencer within the global health architecture. They integrate feedback from Unitaid, the I4TB consortium, and other key stakeholders consulted as part of the evaluation. Expanded recommendations are included in the full evaluation report.

Part 1. Recommendations for Unitaid's investments in TPT

These recommendations consider key trends relevant to TB services, notably the significant shift in the TB funding and implementation context, emerging technologies that bring TB diagnosis closer to communities, including near-point-of-care (NPOC) and tongue swabs which are recommended in the latest Global Fund guidance for Grant Cycle 8, and Unitaid's strong credibility within the TB community through I4TB and its wider TB portfolio and engagement.

Recommendation 1: Consolidate remaining I4TB gains by (i) accelerating policy uptake relevant to priority populations, and (ii) supporting regional API manufacturing

- Unitaid should collaborate with WHO to rapidly translate the forthcoming DOLPHIN-Moms and DOLPHIN-Kids evidence into updated global guidance and support timely country dissemination, in collaboration with TAG and other partners.
- Unitaid should collaborate with the Global Fund, WHO and civil society to support countries to incorporate forthcoming WHO guidance into Global Fund Grant Cycle 8 planning and national policies, using existing TB investments and partnerships to provide technical assistance, where needed. This approach is already being applied through Unitaid's Advanced HIV Disease grant to Aurum and other Aurum-led TB activities.
- Unitaid should assess the early results of investment with CPT Pharma and identify opportunities for continued support if promising. This could be linked with Unitaid's other regional manufacturing efforts.

Recommendation 2: Integrate TPT with new TB screening, diagnostics and community-based delivery to close the gap in TPT uptake - supporting more integrated, people-centred approaches for priority populations

- Unitaid should promote integration of TPT into community-based TB screening and diagnostic pathways, using portable digital X-ray/CAD in the near term, and emerging near-POC diagnostics and simplified specimen collection approaches as they become available.
- Unitaid should support implementation models that strengthen contact investigation and active case finding, recognising these are now among the principal constraints to expanding TPT.
- Unitaid should continue prioritising integrated, people-centred approaches that bring TB services closer to vulnerable populations.

Recommendation 3: Sustain Unitaid's leadership in developing TB prevention and treatment options for underserved populations, including children and pregnant women

- Unitaid should explore strategies to accelerate country availability of child-friendly formulations. This could include engaging civil society for national advocacy and country support to address bottlenecks in product registration.
- Unitaid should build on I4TB lessons from paediatric market shaping. Where achieving price parity with adult formulations is not feasible, explore mechanisms to incentivize inclusion of child-friendly products in domestic financing strategies, and in Global Fund and other financing mechanisms.

Recommendation 4: Leverage Unitaids influencer role to ensure TPT and complementary activities are covered as high burden countries plan for the transition to domestic financing

- Unitaids should bring the lessons learned from I4TB and other TB prevention projects, and its credibility in demand forecasting to inform national and subnational planning and budgeting processes. In some cases, it may be strategic for Unitaids and/or its partners to participate directly in domestic financing discussions.

Recommendation 5: Continue to position Unitaids for the next generation of TB prevention innovations

- Build on Unitaids leadership in TB prevention by convening partners around future TPT innovations and preparing for TB vaccine introduction. Use Unitaids convening role to help clarify delivery models, financing approaches and country readiness for future TB prevention technologies.

Part II. General recommendations for Unitaids across investment areas

The following cross-cutting recommendations draw from the market shaping and CCSE learning themes and other evaluation insights. and reflect the current health financing context.

Recommendation 6. Continue investing in integrated access strategies where relevant

- I4TB's effectiveness stemmed from addressing multiple barriers to rifapentine access simultaneously, including supply constraints, limited clinical evidence, lack of child-friendly formulations, weak demand, and policy hesitancy. Future Unitaids investments should consider this comprehensive approach, acknowledging I4TB's comparatively large value within Unitaids portfolio.
- Future investments should strengthen alignment between supply and country demand activities, informed by robust review of production capacity and risks. This is particularly critical where there is a single supplier. The EMAN is a good example of aligning country readiness (e.g. policy) with supply.

Recommendation 7: Evolve Unitaids grant-making to improve speed and agility, whilst retaining Unitaids flexibility within project delivery

- Unitaids should test more co-creation and flexible approaches to project development with implementing partners. This could include (i) targeted expressions of interest based on partner landscape analysis and early engagement; (ii) small number of strategic portfolio partnerships that provide a flexible 'call-down' mechanism, improving agility and reinforcing Unitaids catalytic role. To inform such options, Unitaids could scope the grant-making approaches of other organisations having a similar catalytic role. This could also inform early analysis for Unitaids future strategy.
- Unitaids should continue enabling projects to adapt as evidence and implementation experience evolve, which was considered a strong value-add within I4TB.
- Unitaids should continue to encourage consortia with leadership based in the global South and maintain a strategy-level KPI to monitor progress.

Recommendation 8: Address bottlenecks to shorten the pathway from evidence generation to policy impact

- Unitaids should review the value for money of its evidence generation approach to identify the mix of research approaches that delivers the greatest policy influence and country uptake.
- Unitaids should explore where appropriate, a greater emphasis on evidence generation approaches such as operational and implementation research that can more rapidly inform country policy and programme decisions. Such research should leverage and strengthen national data systems, using routine and real-time data to support adaptive implementation and accelerate learning.
- Unitaids should also work with the WHO Ethics Review Committee (ERC) to identify and address the main constraints within review processes without compromising scientific rigour.

Recommendation 9: Strengthen integrated, people-centred investment portfolios and the use of gender-based approaches

- New investments should consider opportunities beyond disease ‘silos’, drawing on resources such as Unitaids recent landscape analysis of care pathways for populations at higher risk of tuberculosis. Unitaids is also supporting this through forthcoming integrated diagnostics investments.
- Strengthen gender and equity analysis during investment design and implementation, including routine use of sex-disaggregated data to identify gaps across the service cascade.

Recommendation 10: Continue to embed CCSE in Unitaids work, with implementation timelines and financing that reflect the contribution to project outcomes

- CCSE contribution to project outcomes should be strengthened within results frameworks. Future investments should also explore more sustainable funding models than one-off grant cycles, strengthening organisational capacity where needed, and promoting longer-term financing mechanisms such as social contracting where appropriate.

1. INTRODUCTION

Cambridge Economic Policy Associates (CEPA) was appointed by Unitaid to conduct an end-of-project evaluation of Unitaid's investment in "Enabling Tuberculosis Preventive Treatment (TPT) in High-Risk Populations" encompassing a US\$78m to Aurum Institute and partners to catalyse access to short-course TPT for People Living with HIV/AIDS (PLHIV) and child contacts along with a number of complementary investments.

This first section provides the investment background (Section 1.1), evaluation objectives, framework and methodology (Section 1.2).

1.1. OVERVIEW OF UNITAID TB PREVENTION INVESTMENT

Tuberculosis (TB) remains the world's leading infectious killer. In 2024, 10.7 million people became infected with TB and 1.23 million died.³ Worldwide, one in four are infected with TB bacteria, however only 5-10% will go on to develop active TB disease. Preventing this progression is a cornerstone of the World Health Organization (WHO) Global End TB Strategy (2015-2035). WHO recommends TPT for those most at risk: PLHIV, household contacts of people with active TB disease, and other high-risk groups, supported by effective screening, early diagnosis, and prompt treatment.

Despite global guidance on TPT, uptake was historically limited. Key barriers to effective TPT were the long duration of existing regimens (6-36 months) which were impractical and difficult to deliver in resource-constrained settings. A major advance came through the emergence of shorter rifapentine-based options such as 3HP and 1HP, first recommended by WHO in 2018.⁴ However scale-up commitments from countries and health financing partners lagged due to several factors: unresolved questions on potential drug interactions with dolutegravir for PLHIV, a priority population for TPT initiation⁵; a highly constrained market with high costs (around US\$ 72 per adult course) with only the originator supplier (Sanofi) and insufficient production capacity⁶; and uncertainty on how best to deliver the shorter regimens within the health system in high burden countries. The absence of a fixed-dose combination (FDC) of rifapentine and isoniazid for 3HP/1HP regimens also meant an increased pill burden, raising concerns about acceptability and treatment completion.

To address these challenges, Unitaid launched the 'Increasing Market and Public Health Outcomes through Scaling Up Affordable Access Models of Short Course Preventive Therapy for TB (IMPAACT4TB)' (I4TB) project in 2017, led by the Aurum Institute. Details for the IMPAACT4TB project in terms of the project goal, outcomes and outputs are described in Table 1.1. A costed extension to the original project was made in 2022 to address further priority TPT access barriers for children and pregnant women.

³ The burden of TB is concentrated in Southeast Asia (34%), Africa (24%), and the Western Pacific (27%). Source: WHO (2025) Global Tuberculosis Report.

⁴ 3HP is a combination of two drugs, rifapentine and isoniazid, which are taken once weekly for 3 months to kill latent TB infection, preventing progression to active TB disease. 1HP is one month of treatment of daily isoniazid and rifapentine. Source: IMPAACT4TB Clinical Guidelines.

⁵ There were initial concerns that 3HP would cause drop in dolutegravir levels large enough to cause sub-therapeutic exposure, increasing the risk of viral rebound, treatment failure, and the development of HIV drug resistance. This concern was based on a previous 2018 study of 3HP use among HIV negative volunteers which had found a modest reduction in dolutegravir concentrations. This study had been stopped early due to adverse events in two out of four participants. Source: Conference on Retroviruses and Opportunistic Interactions (CROI) 2019 Abstract. Available at: <https://i-base.info/htb/35823>

⁶ Treatment Action Group (2018) TB prevention pipeline report. Available at: www.treatmentactiongroup.org/wp-content/uploads/2019/06/pipeline_2018_tb_prevent_mf_web2.pdf

Table 1.1: IMPACCT4TB project goal, outcome and outputs (including grant extension)^{7,8}

Aspect	Detail				
Goal	To reduce TB incidence and deaths among PLHIV and child contacts through sustainable implementation of affordable, quality-assured 3HP				
Outcomes	Increase the number of PLHIV (15-49) and child contacts <5 years starting treatment with affordable, quality-assured 3HP; and contribute to revising WHO preventive therapy guidelines based on evidence generated.				
Project outputs	Output 1: Establish a price agreement for Rifapentine with the innovator in the short term and with generic manufacturer(s) in the long term (global level)				
	Output 2: Accelerate development and filing of Rifapentine with a global level SRA (WHO PQ and/or FDA) and country National Drug Regulatory Agencies (NDRAs), through an incentive grant, by generic manufacturer(s) (global level) <i>Extension Output 2: To support the development and create demand for child friendly formulation of RPT 150mg tablet, which is functionally scored (FS) and fully dispersible (DT).</i>				
	Outputs 3-4: Initial scale up of 3HP for PLHIV supported and for child contacts supported (country level) <i>Extension Outputs 3-4: To support the scale up of short and ultrashort course TPT regimen using 3HP or 1HP for PWHIV, HIV-uninfected HHCs adults and children >2.</i>				
	Output 5: Evidence generated and disseminated for optimal use of 3HP and scalable models of delivery (global and country level) <i>Extension Output 5: To generate evidence for policy and collaborate with WHO on the programmatic management of latent TB infection.</i>				
	Output 6: Engage with WHO to ensure the successful implementation of the IMPAACT4TB and other Unitaid TB projects (at a global level)				
Grantees	Aurum Institute (lead), Implemented with CHAI, KNCV, Johns Hopkins University (JHU), Treatment Action Group (TAG)				
Timeline, budget and objectives	Duration	Budget	Key objectives	Focus countries	
	Original grant 2017-2021	Original US\$ 58.9m	To catalyse access to short-course TPT for PLHIV and child contacts by removing critical market and access barriers and creating the conditions for sustainable scale-up	12 high burden countries: Brazil, Cambodia, Ethiopia, Ghana, India, Indonesia, Kenya, Malawi, Mozambique, South Africa, Tanzania, and Zimbabwe	
	With no cost extension 2021-2022				
	Costed extension 2022-2024	With cost extension US\$ 78.0m	To increase the number of child and adult household contacts (HHCs) and PLHIV started on TPT and contribute to the revision of WHO guidance		
	No cost extension 2024-2025				
	Total period: 8 years, 4 months	Total budget US\$ 78.0m			

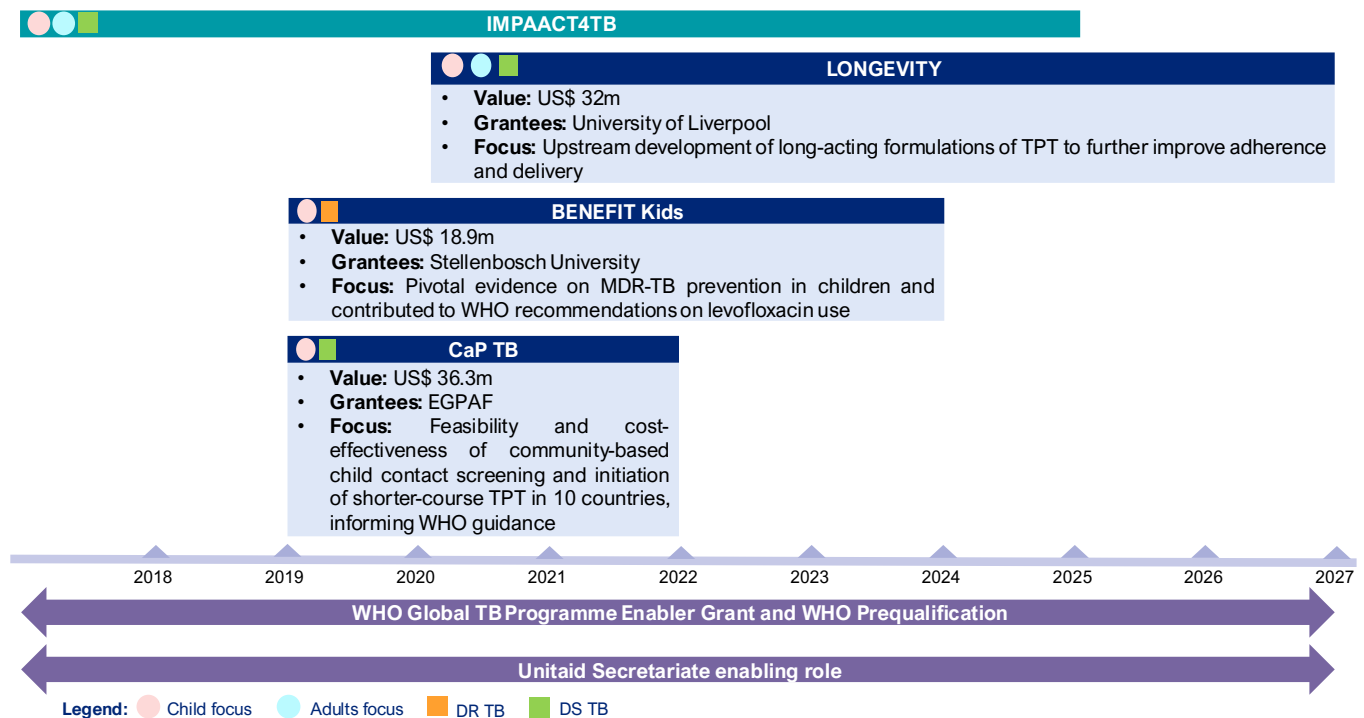
The flagship IMPAACT4TB (I4TB) project formed part of Unitaid's broader TB prevention portfolio, which comprised multiple complementary investments targeting different population groups and both drug-sensitive (DS) and drug-

⁷ Unitaid (2025), Terms of Reference Portfolio Evaluation: Enabling preventive TB treatment in high-risk populations, Unitaid (2022), Annex 1C, Project Plan Amendment, Unitaid, Annex1f, Project Plan Amendment

⁸ Unitaid (2023), Flash Report Data. Available [here](#).

resistant (DR) TB (Figure 1.1). The portfolio also included several cross-cutting enabling investments, such as support to the WHO Global TB Programme and WHO Prequalification, aimed at accelerating the adoption of new TB drugs and formulations and strengthening normative guidance. In addition, the Unitaid Secretariat played an active enabling role in supporting TPT scale-up, including by identifying and leveraging partnerships with the Global Fund and PEPFAR to secure lower rifapentine prices and advocating for wider adoption of rifapentine-based regimens.

Figure 1.1: Unitaid investments in TB prevention portfolio (in addition to I4TB)⁹



Source: CEPA analysis

1.2. EVALUATION OBJECTIVES AND METHODOLOGY

Evaluation objectives and scope

This objectives of this end-of-project evaluation are to:

- provide an independent assessment of the extent to which the I4TB project and Unitaid's complementary investments in TB prevention contributed to accelerating access to quality-assured, affordable TPT for high-risk groups and key lessons learned – the evaluation covers all OECD DAC evaluation criteria, but focuses on the criteria of **effectiveness, scalability, impact and sustainability**.
- support internal Unitaid learning by assessing the extent the investment contributed to Unitaid's strategic role as a pathfinder, investor, and influencer (noting the project was developed prior to the Unitaid 2023-27 strategy in which these roles were formally prioritised).

⁹ Unitaid also has ongoing investments promoting innovative use of TRIPS (Trade-Related Aspects of Intellectual Property Rights) flexibilities and supporting the Medicines Patent Pool to improve access to medicines. While this work was not explicitly identified by stakeholders as contributing to I4TB during the evaluation, there are clear linkages with TRIPS flexibilities investment in that TAG, an I4TB consortium member and grantee under Unitaid's TRIPS flexibilities work, developed a *3HP Access Roadmap and Patent Landscape* in 2020 to inform TB advocates, procurement agencies and generic manufacturers about the intellectual property landscape for rifapentine-based TPT.

As a **learning focused evaluation**, the evaluation includes two specific learning themes on **community and civil society engagement (CCSE)** and **market shaping**. It also examines what worked, and what didn't work, and why to inform future Unitaid investments in TB prevention and beyond.

In terms of **scope**: the evaluation primary focus is the I4TB investment as the largest investment within the TB prevention portfolio but it also considers Unitaid's other TB prevention projects for aspects such as coherence and contribution to Unitaid's intended outputs, outcomes and impact as outlined in the theory of change (ToC) included in Appendix A).

Evaluation framework, theory-based approach and methods

This is a theory-based evaluation using contribution analysis, drawing on the ToC for Unitaid's '*Enabling preventative treatment in high-risk groups*' portfolio, which includes IMPAACT4TB and complementary investments.

A high-level evaluation framework is shown in Figure 1.2 (refer to Appendix A for the full evaluation framework). Several key points should be noted. First, the effectiveness assessment groups the five priority Unitaid access barriers into two distinct components. This reflects the strong interdependence between interventions addressing these barriers and enhances coherence in the evaluation. The two components are: **(i) supply-side interventions**, covering the innovation and availability, affordability, supply and delivery, and quality access barriers; and **(ii) demand and adoption**. Second, the remaining OECD DAC evaluation criteria are grouped in a way that reflects both the specific characteristics of the I4TB project and Unitaid's priorities for this evaluation.

Figure 1.2: Summary evaluation framework

OECD DAC Evaluation Criteria	Evaluation question topics	Key learning themes
Effectiveness	1. To what extent have IMPAACT4TB & complementary investments accelerated progress against the TAP for rifapentine-based TPT & achieved their key objectives as per access barriers of: 1a. Innovation and availability, Affordability, Supply and delivery, Quality 1b. Demand and adoption	Community and Civil Society Engagement Market shaping
Scalability Sustainability Impact	2. Contribution to global and country readiness for scale 3. Dissemination of knowledge, evidence and lessons on equitable access, and effects 4. Impact and sustainability of progress achieved, and gaps remaining 5. Contribution to regional manufacturing and greener API products	
Relevance Coherence Efficiency	6 Extent IMPAACT4TB is doing the 'right things' – including community responsiveness, adaptation and equity and inclusion 7. Coherence and value add with respect to IMPAACT4TB and other TB prevention efforts 8. Efficiency in execution	

Evaluation methods and robustness assessment

Evaluation methods are summarised in Figure 1.3. Qualitative evidence from all sources was analysed using a structured framework aligned with the evaluation questions. Findings were triangulated across sources to identify areas of convergence and divergence. To ensure transparent interpretation, each key finding is assigned a four-point strength-of-evidence rating (high, medium, low, or insufficient), reflecting the quantity and quality of evidence and the extent of triangulation. Appendix A provides further details on the robustness assessment and scoring rubric.

Figure 1.3: Mixed evaluation methods



Document review

- Grant documents and project reporting
- Complementary TB investment and Unitaids strategy materials
- Key global materials, including WHO guidelines and partner documentation
- Academic and grey literature on TB prevention



Stakeholder & focus group interviews

- 96 stakeholders interviewed, including 33 at global level and 62 at country and regional level
- AI to summarise interview notes against a structured framework, with human verification



Country case studies

- Three in-depth studies in Indonesia, Cambodia and Zimbabwe
- Five light-touch country assessments* across Brazil, India, Malawi, Mozambique, Tanzania



Thematic case studies

- Civil society engagement and market shaping as two focused learning themes through key questions
- Triangulated with project documentation, consultations and reporting

**Scope originally included Pakistan, however stakeholders were not available during the evaluation period. In Brazil, the review was based predominantly on documentary evidence due to stakeholder unavailability*

Limitations and mitigations

Limitations and mitigations are described in Table 1.2.

Table 1.2: Limitations and mitigating actions

Limitations	Mitigating actions
Substantial length of time elapsed since the close of the main I4TB project in 2022, implicating both assessment at the country level, and of the supply-side market intervention, as some key stakeholders closely engaged in I4TB have moved on and are no longer available. The evidence is also subject to potential recall bias.	Larger emphasis in the evaluation on documentary evidence, including from Aurum project reporting and dissemination materials, and from global sources such as from WHO.
Country level assessments were also affected by recall and availability, with many stakeholders involved in planning for the Global Fund Grant Cycle 8 during the evaluation period. No interviews were able to be conducted in Pakistan (a 'spillover' I4TB country) or concerning I4TB activities in Brazil despite the evaluation team's best efforts.	Project reports, national and global data were used to triangulate consultee evidence and fill key gaps.
Some project documentation is only available until 2022 (e.g. country project data).	Data for recent years was obtained through publicly available sources such as WHO reports, noting there are limitations to the level of disaggregation in country reporting to WHO.

2. FINDINGS

This section presents the evaluation findings by OECD DAC evaluation criteria and key evaluation questions, in line with the evaluation framework. Call-out boxes marked with  contain the two priority learning themes along with other key insights identified through the evaluation, and those with  provide examples from the case studies.

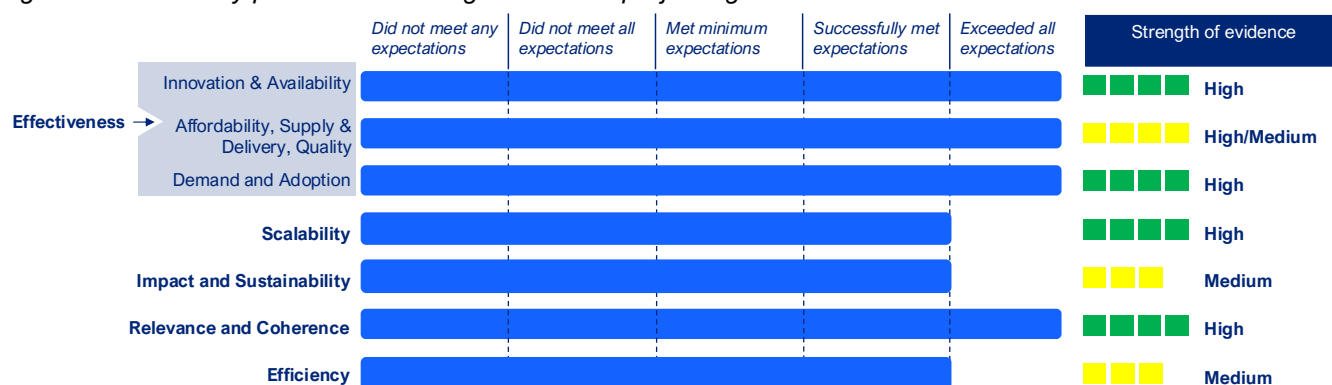
2.1. SUMMARY ASSESSMENT OF PROJECT PERFORMANCE

A summary assessment of performance against the OECD DAC evaluation criteria is shown in Figure 2.1. This is based on a 5-point scale adopted by Unitaid as follows: (1) exceeded all expectations; (2) successfully met expectations; (3) met minimum expectations; (4) did not meet all expectations; and (5) did not meet any expectations.

I4TB can be considered a highly successful Unitaid investment, exceeding expectations in terms of addressing priority access barriers to rifapentine-based TPT and its relevance and coherence, and meeting expectations across the remaining OECD DAC evaluation criteria. Assessment of scalability, which examines catalytic impact post-I4TB support at country level, reflects a more mixed picture. This includes substantial up-take since the project started, including other countries adopting TPT during project implementation however there has been slower-than-expected scale-up of household contact TPT and a plateau in TPT initiation among PLHIV, which reached 58% in 2024—well below the global target of 90% coverage by 2027.

I4TB achievements are the result of strong stakeholder engagement and coordination at global and country level, both by I4TB and Unitaid's direct engagement. Unitaid played a strong influencer and pathfinding role across key project components – including in market shaping and evidence-generation, in addition to Unitaid's significant investor role. This assessment and the details behind it are discussed in the subsequent sections.

Figure 2.1: Summary performance rating of the I4TB project against OECD DAC evaluation criteria



2.2. EFFECTIVENESS

1. To what extent did the IMPAACT4TB investment and other complementary investments accelerate the development and introduction of quality-assured, fit-for-purpose tools to improve access to TPT in LMICs for high-risk populations and lead to progress against the Target Access Profile¹⁰ (TAP) for rifapentine-based TPT? Did the investment effectively identify and remove critical access barriers?

¹⁰ Unitaid uses Target Access Profiles (TAPs) to define and track the desired access conditions required for products to become readily accessible for the people and communities who need it most. Targets are specified for access conditions across the barriers of innovation & availability, quality, affordability, demand & adoption, and supply & delivery.

I4TB employed a comprehensive market shaping approach to address both demand and supply related access barriers to TPT. A summary of targets and achievements for each access barrier is shown in table 2.1. Assessment of the effectiveness of I4TB market shaping, and complementary Unitaaid investments, is structured around two pillars as follows:

- **Market supply shaping interventions**, covering Unitaaid access barriers of (i) innovation and availability; (ii) affordability; (iii) supply and delivery; and (iv) quality; and
- **Market demand and adoption interventions**, covering demand-related access barriers including with regards to policy and uptake at both global and country levels.

Table 2.1: Summary of I4TB key access barriers, project targets and achievements¹¹

Access barrier	Targets	Key achievements
 Innovation & availability	2 new generic RPT products filed with global SRA (WHO PQ and/or FDA) and country National Drug Regulatory Agencies (NDRAs)	3 generic products: Macleods and Lupin both secured WHO PQ for FDC, 300mg, and paediatric-friendly formulation Filed in 25 unique countries: 18 (Lupin), 25 (Macleods). Note: May not reflect latest country filings
 Affordability	End of project US \$10 'target', catalysed through: • Price agreement with Sanofi • Price agreement with generic(s) in the longer term	Achieved Sanofi pricing agreement of US\$15 (2019), and later with 2 generics (MacLeod's and Lupin) Price of 3HP course has overall reduced by 86% , from US\$72 (pre-project) to ~\$US9.99 (2026)
 Supply and delivery	Maintain supply security and affordable pricing of rifapentine products through entry of generic(s) and support for demand forecasting - no specific target	Annual production capacity is now >5 million courses across all suppliers, a substantial increase from 2017 capacity of 0.50.6 million courses under single supplier
 Quality	100% of Aurum-procured 1HP and 3HP batches cleared of nitrosamine issues	Varied by year. 100% in 2024. Note: API impurities are generally a risk for all RFP products
 Demand & Adoption	Evidence generated on 3HP use among priority populations Countries including 3HP in TPT guidelines for PLHIV: 12 I4TB countries plus 20 additional countries through catalytic effect of I4TB 462,228 PLHIV initiated on 3HP in I4TB target sites	9 WHO policies and guidelines informed by I4TB evidence to date In all 12 I4TB countries , 3HP is approved in guidelines for both the HIV and TB programs. 59 'catalytic effect' countries 123,648 initiations (27% of target) in target sites, with additional 504,000 initiations through catalytic impact in 12 I4TB countries beyond target sites Note: Lower 3HP initiation in project target sites largely reflects delays from COVID-19 impact, impurity issues, and supply constraints due to lower manufacturing capacity than anticipated over 2020-2022

Performance assessment

 Met objectives

 Met most objectives

2.2.1. Supply shaping

This section assesses the effectiveness of the I4TB market supply shaping interventions in addressing key market barriers to rifapentine-based TPT, through four evaluation questions:

1a. Supply shaping questions:

Innovation and availability. To what extent did the investments address evidence gaps on safety and effectiveness of use for key populations and address access barriers regarding child-friendly formulations?

Affordability. How effective were the market shaping interventions in reducing the cost of 3HP? How effective are the delivery methods in efficiently and cost-effectively reaching the target population within the project, and how applicable are they beyond the project?

Supply and Delivery. How effective have the investments been in increasing supply security and improving supply chain systems?

Quality. How effective were the investments in ensuring quality-assured RPT formulations and in addressing API impurities?

¹¹ Source: I4TB project log frame and reporting 2022-2025

In 2018, based on preliminary study results, WHO included 3HP in guidelines for the management of TB/HIV co-infection, an important step for influencing national policy in most high burden countries.¹⁴ Critically from a market shaping perspective, stakeholders also point to this evidence as the precursor to PEPFAR - the largest HIV funder - agreeing to procure 3HP and include the regimen in its technical considerations. Together with negotiations with PEPFAR on 3HP affordability, the DOLPHIN study evidence was a key enabler of market confidence. The DOLPHIN trials were not originally included in Aurum's proposal to Unitaid but added during grant development, evidence of Unitaid's influence in shaping I4TB's design and laying the groundwork for demand.

Further studies on the safety of 3HP among children and pregnant women were later implemented under I4TB to expand this evidence base to other priority populations (discussed further in demand and adoption section 2.2.2).

Finding 2. The supply side interventions under I4TB effectively lowered the price of rifapentine by over 70%, catalysed market entry of FDC products and strengthened supply resilience through market diversification.

Strength of evidence	Rationale
 High/Medium	Strong overall evidence underpinning the headline finding 2, with mix of strong and medium evidence-base for the sub-findings. This reflects uneven stakeholder awareness on the different market interventions, some limitations in the documentary evidence base, and that some stakeholders closely involved in early market shaping were not available.

Unitaid played an important role in orchestrating alignment among key stakeholders around a shared strategy for 3HP scale, including direct engagement with PEPFAR on 3HP affordability. This was critical to secure donor commitment, send positive demand signals to manufacturers, and convince countries on affordability.

- At the time of the start of the I4TB project, stakeholders indicated that different global health donors were engaged with Sanofi directly with mixed messages and confusing market signals to the manufacturer. As a result, Sanofi was unable to effectively plan its supply line. A few stakeholders involved early in the project stated that Unitaid directly played a **leading influencer role** in addressing affordability access barriers, where Unitaid's added value was described as its ability to convene and coordinate actors including Sanofi, PEPFAR, the Global Fund, iPlus solutions, CHAI, MedAccess and PAHO.
- A breakthrough was achieved with PEPFAR announcing that it would purchase 3HP at US\$ 15 per adult course as a threshold for scale. One stakeholder positioned PEPFAR's condition for the US\$ 15 price point as setting the parameters for price negotiations ("*no 3HP if there's no road to scale*" – PEPFAR). This evidence is supported by PEPFAR 2018 Country Operational Plan (COP) guidance requiring countries to strengthen integration of TB/HIV services and reporting on TPT indicators.¹⁵
- PEPFAR's signal enabled Unitaid to enter into an adjustable purchase order with Sanofi, consisting of 900,000 packs of rifapentine and linked to an annual supply cap of 1.8 million packs at the price of US\$ 15 per treatment course and for a period of 12 months (The selection of this market shaping instrument is discussed in the learning brief at the end of this section. Appendix G lists all market shaping tools employed and their rationale within I4TB). Eligible countries included LICs, LMICs, UMICs with a high TB or TB-HIV

¹⁴ Policy adoption in India came later, following review by India's national regulatory authority.

¹⁵ PEPFAR 2018 Country Operational Plan (COP) guidance noted progress on TPT for PLHIV had been slower than other clinical care areas and introduced mandatory reporting on TB screening of patients on ART and the two mutually exclusive clinical decisions from screening: initiation and completion of TB preventive therapy and initiation of TB therapy; 3HP and IPT were included as example TPT regimens Source: <https://www.kff.org/wp-content/uploads/2021/12/PEPFAR-2018-COP-ROP-Guidance-Final.pdf> (Accessed: 1 May 2026).

burden, and selected UMICs. For the first time rifapentine was available to a large number of countries, and with PAHO support, the agreement expanded to include additional Latin American countries.

“From the \$72 per patient cost down to \$15 was one of the reasons that the government eventually came to agree that we can move to shorter regimens.” (Tanzania stakeholder)

However, I4TB did not anticipate a rapid and massive increase in demand, which resulted in early supply shortages. Supply was tightly managed through a highly effective procurement coordination group.

- Within a few weeks of Unitaids’ agreement with Sanofi, there was demand of 3 million 3HP courses (Sanofi production capacity at this time was an estimated 500,000 to 600,000 adult courses per year), spurred on by the UN High Level Meeting (UNHLM) targets, particularly to initiate 6 million PLHIV on TPT over 2018-2022, and extensive demand generation work by the Global Fund country teams and PEPFAR in countries. Project reporting by Aurum¹⁶, corroborated by stakeholder interviews, describe supply disruptions, such as in Kenya where delays in procurement and deliveries affected national scale-up of 3HP. In Malawi, Aurum reported that TPT services were temporarily suspended due to drug expiry and delayed restocking.¹⁷ Sanofi was unable to meet this demand surge and there were no further suppliers in the market at this time; as a result, supply had to be effectively rationed across countries. In addition, further supply issues were faced with API impurity issues of nitrosamine identified with the Sanofi rifapentine product in 2020 (see Box 1).¹⁸
- **To facilitate demand coordination in the context of limited supply, a highly effective procurement coordination group was constituted in 2020** –the well-functioning existing ARV procurement working group was repurposed to support coordination of procurement for rifapentine-based TPT.¹⁹ Sanofi agreed to a streamlined list of eligible procurement channels (Global Fund/PPM (through iPlus Solutions), GDF/IDA, MSF, NDOH Republic of South Africa, PAHO, USAID/GHSC-PSM) to ensure prioritized access to 150mg rifapentine in eligible countries.²⁰ Together, these countries represented more than 90% of estimated global need for TPT. Unitaids, iPlus Solutions, CHAI and many others played a key role in this working group to coordinate procurement. There were significant supply security efforts including coordination of procurement, readiness management (e.g. only shipping the product to countries that were ready to implement), and reallocation of Unitaids’ own volumes *“just to make sure that as many countries as possible got the product”*. During this period, GDF also utilized the USAID-funded Strategic Rotating Stockpile (SRS)²¹ to supplement where needed to avoid stockouts. Real-time data on TPT distribution and demand forecasts were also made available through various country teams. This helped prevent one country or buyer from taking a disproportionate share of limited stock and supported phased allocation based on programme readiness. **The work of the procurement coordination group built on important lesson learned from previous engagement with Sanofi in terms of the value of a single line of communication with the supplier, alongside improved communication with country programmes.**

¹⁶ Aurum (2023), Scale-up of short-course TB preventive treatment (3HP) in high tuberculosis burden countries: Experiences from the IMPAACT4TB Project.

¹⁷ Supply security issues constrained early country implementation where I4TB CSO partners had begun working at community and national level to create demand for new TPT regimens but had insufficient product. Source: An Evaluation of the 3HP TB Preventive Therapy Demand Creation and Advocacy Project carried out by Civil Society Organisations under the IMPAACT4TB Grant during the Period 2020-2021 in High TB-burden Countries.

¹⁸ <https://extranet.who.int/prequal/news/nitrosamine-concerns-rifapentine-and-rifampicin>

¹⁹ The ARV procurement working group expanded its focus to cover rifapentine-based TPT as the focus population group for TB prevention was PLHIV and hence the product was not considered as a TB molecule but an HIV product.

²⁰ Unitaids (2019), Sanofi rifapentine (priftin) global price discount for year 2020.

²¹ GDF operates a Strategic Rotating Stockpile (SRS) to reduce delivery lead time, mitigate the effects of supply chain disruptions on product availability and to stabilise global markets.

Unitaid is described as playing a key influencer role in shaping the market towards a 3HP FDC formulation and in maintaining the US\$ 15 3HP price ceiling for FDCs manufactured by generics entering the market, diversifying the supplier base and increasing production capacity.

- Simultaneous to the engagement and negotiations with Sanofi, we understand that all actors were involved in developing the Target Product Profile (TPP) for rifapentine-based TPT.²² Unitaid in particular pushed strongly for this to prioritise a FDC formulation (rather than 300mg rifapentine) which served as a market signalling step for the generics and ultimately led to the generic FDC products that came into the market beginning in 2022.
- Under I4TB, CHAI launched an RFP for manufacturers for the 3HP FDC, with Macleods and Lupin responding (both India-based generics pharmaceutical companies). Macleods in particular has a longstanding focus on TB products and substantial experience in developing treatments for adult and paediatric TB, drug-sensitive and drug-resistant TB, as well as expansion into HIV and malaria products. Macleods intimated that they identified the need for 3HP through secondary research and clinical analysis, beginning development in as early as in 2017, taking a calculated risk to invest in the product before it became widely recognized. When Unitaid announced a grant for 3HP development through the I4TB project, Macleods had already started to develop their product, and therefore the grant funding under I4TB was used for expediting WHO pre-qualification and commercialization rather than initial development. This was regarded as value added support from Unitaid, noting the company's longstanding expertise in TB drug development.
- Unitaid and CHAI (under I4TB) agreed with Macleods in February 2021 that it would launch 3HP FDC at US\$15 across 138 LMICs. The FDC was seen as a strong value proposition because programmes did not need to buy isoniazid separately and would reduce the pill burden for people taking TPT.²³

Supply was impacted by COVID-19-related disruptions and delays in achieving a WHO prequalified FDC product. MedAccess' subsequent volume guarantee (VG) to signal continued demand and support market stability was strongly complementary to Unitaid and I4TB's 'first-mover' market interventions and contributed to a further price reduction.

- Pre-qualification of the Macleods FDC was achieved later than anticipated on account of a number of issues including with regards to manufacturing scale-up, yield loss, and impurity-related testing (nitrosamine) (see Box 1). It wasn't until May 2022 that Macleods became the first supplier to receive WHO pre-qualification for its 3HP FDC adult product (300mg rifapentine/ 300mg isoniazid).
- Following supply disruptions in 2020 due to COVID-19-related force majeure declared by Macleods, CHAI negotiated an amendment to the agreement in April 2021. This amendment extended the ceiling price period and revised supply commitments to reflect updated market conditions. In August 2021, MedAccess then executed a volume guarantee with Macleods, alongside CHAI and Unitaid, to extend this access pricing and support scale-up of Macleods' production capacity to around 1.5 million patient courses in 2021.^{24,25}

²² WHO (2020). Target product profiles for tuberculosis preventive treatment.

²³ Unitaid (2021), New patient-friendly tuberculosis preventive treatment to be rolled out in five high-burden TB countries at affordable prices.

²⁴ MedAccess. Improving availability of patient-friendly tuberculosis preventive therapy.

²⁵ For Macleods, Unitaid also negotiated with MedAccess so that the volume guarantee fee would not be built into the product price but instead paid for separately as a service. This reduced the proposed MedAccess fee from around \$1.2 million to about \$500,000–\$550,000 to maximise use of the budget.

The arrangement was later updated in 2022, reducing the ceiling price further to US\$14.25 per course.^{26,27}

- Supply further diversified over 2023-2024 with availability of 1HP FDC (Macleods, September 2023). Lupin's 3HP FDC was similarly delayed due to API impurity issues but ultimately achieved WHO PQ for its 3HP FDC in October 2024 (table 2.1).



Box 1. I4TB played a key role in ensuring the quality of rifapentine-based TPT and to conserve confidence in 3HP when nitrosamine impurities were detected

All countries benefitted from I4TB's global efforts to ensure the quality of rifapentine-based TPT. The project worked with new manufacturers to prepare for WHO PQ and set up quality assurance systems. Additionally, I4TB entered into a short-term agreement with FHI 360 to provide batch testing until Lupin and MacLeod's had capacity to provide testing.

When nitrosamine impurities first arose in 2020 with Sanofi's product²⁸, quality concerns delayed shipments and, in some cases, resulted in a recall of 3HP regimens that had already been delivered to focus countries.

An impurities Task Team was formed by Aurum, WHO, GDF and CHAI and met every 2 months to review nitrosamines in rifamycin products. The group aligned on messaging so that all stakeholders, including country teams, were up to date on the issues. IMPAACT4TB and WHO developed briefing materials for users and maintained close communication channels to explain risks and guidance. Messaging focused on reassuring that current impurity levels were considered acceptable and preventing loss of confidence in rifapentine-based regimen.

Nitrosamine impurities also emerged later in the project in relation to Lupin's product and have remained an ongoing area of concern and scrutiny.

As such, market shaping interventions that led to Macleods market entry and price reduction included a mix of both the development incentive from Unitaid/ CHAI through the I4TB project and the MedAccess volume guarantee (also supported by CHAI and Unitaid). This also represented strong complementarity between Unitaid's initial market intervention that significantly lowered the price of 3HP and longer term market shaping by MedAccess to signal continued demand and support market stability. Since the initial agreements with Sanofi, Macleods, and Lupin under I4TB, growing demand and additional donor commitments contributed to further price reductions. In 2023, USAID and PEPFAR secured a 30% price reduction for a 3HP treatment course, from US\$14.25 to US\$9.99, available through the GDF. As part of this agreement, the US government committed a combined US\$ 25 million to provide 3HP to 2.5 million people at risk of TB globally, reaching an estimated 750,000 additional people compared with what would have been possible at the previous price. Across the three manufacturers, production capacity increased from 180,000 patient courses in 2018 to over 4.4 million in 2025.

The timeline of product commercialisation for adult and child-friendly formulations and 3HP price reduction over time is shown in Table 2.2 and Figure 2.3.

Table 2.2: Rifapentine-based TPT market supply and timelines²⁹

Product	Manufacturer	PQ Date	Significance
Rifapentine 150mg tablet	Sanofi	Feb 2017	Original product
Isoniazid/Rifapentine 300mg/300mg FDC	Macleods	May 2022	First generic 3HP FDC
Rifapentine 300mg tablet	Macleods	Sept 2023	For 1HP regimen

²⁶ PLOS (2026), Advancing global health access through market shaping: Cases and learnings.

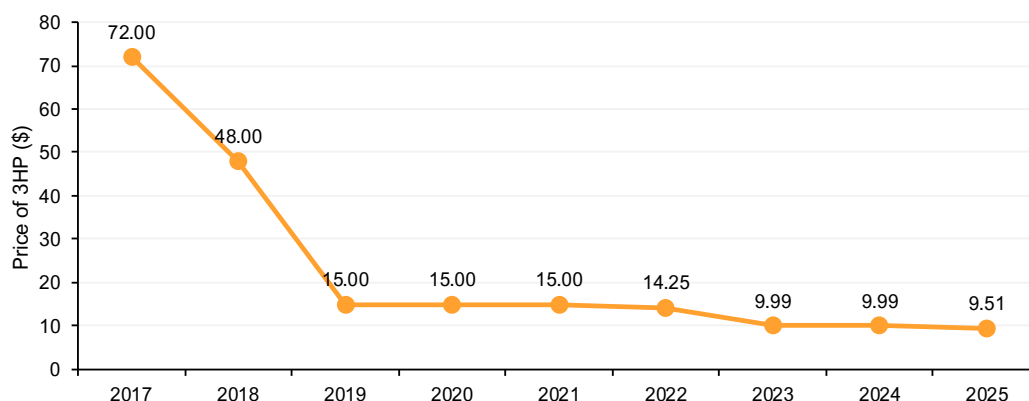
²⁷ Unitaid, Rifapentine Global Pricing Update.

²⁸ WHO (23 October 2020). Nitrosamine concerns for rifapentine and rifampicin. Available at: <https://extranet.who.int/prequal/news/nitrosamine-concerns-rifapentine-and-rifampicin> (Accessed: 3 June 2026)

²⁹ Unitaid (2026), Portfolio Evaluation: Enabling preventive TB treatment in high-risk populations.

Product	Manufacturer	PQ Date	Significance
Rifapentine 300mg tablet	Lupin	July 2024	Second generic supplier
Isoniazid/Rifapentine 300mg/300mg FDC	Lupin	Oct 2024	Second 3HP FDC supplier
Rifapentine 150mg dispersible	Lupin	Nov 2024	Allows for first pediatric formulation (combined with existing pediatric isoniazid)
Rifapentine 150mg dispersible	Macleods	July 2025	Second pediatric supplier

Figure 2.3: Trend in price of adult 3HP course in US\$, 2017-2025³⁰



However, while the supply capacity has developed and there is greater security and resilience in the supply, recent years have seen a plateauing of demand. This is on account of a number of reasons including: completed coverage of PLHIV through TPT (refer to Section 2.3.1 for greater information) and no clear repeat-dosing guidance, challenge in expansion of household contact tracing and active case finding as a means to boost demand, and importantly, the recent decline in global health funding including PEPFAR and Global Fund funding implying limited funding for TPT. Despite the prioritisation of TPT in global guidance, such as inclusion as a ‘Program Essential’ in Global Fund country guidance, stakeholders note that past constrained funding periods have shown diagnosis and treatment investments are more likely to be preserved over prevention efforts. One stakeholder opined the funding context may have a greater impact on efforts to expand household contact tracing, whilst conserving TPT within services for PLHIV and child contacts. The current price of TPT is still not attractive for direct country purchase through domestic budgets (more on this in the section below on demand and adoption and scalability and sustainability).

Finding 3. I4TB was a pathfinder in addressing a key gap in market availability of affordable, quality-assured child-friendly 3HP

Strength of evidence	Rationale
High	Strong consensus from consultations, supported by documentary evidence on Unitaids pathfinding and investor role in child-friendly 3HP.

Through the I4TB project, Unitaids launched an Early Market Access Vehicle (EMAV) to bring a paediatric, dispersible formulation of rifapentine to market (this could be combined with dispersible isoniazid which was already commercially available for 3HP). The EMAV is designed to be more ‘demand-driven’ than alternative instruments for new product introduction and required countries to meet a set of pre-conditions, following which they could apply to obtain access pricing of paediatric-friendly rifapentine (refer to the market shaping learning brief at the end of this section for more details). The EMAV included manufacturer commitments to develop and launch paediatric

³⁰ Unitaids (2026), Portfolio Evaluation: Enabling preventive TB treatment in high-risk populations.

formulations at no higher than the US\$15 price of adult 3HP, with I4TB committing to purchase 85,000 doses. EMAV procurement was channelled through the GDF.

Ultimately Lupin entered into the EMAV agreement and the paediatric product was introduced in November 2024, 15-18 months after the initial Lupin adult 3HP product launch. Lupin's 150 mg scored, dispersible rifapentine was considered a key enabler for child TPT and a "game changer"³¹ for children at risk of TB disease. I4TB's supply shaping intervention for the paediatric-friendly 3HP formulation is an example of Unitaid's contribution through I4TB to addressing access gaps for underserved groups, including children and pregnant women (refer to demand and adoption and relevance findings for further I4TB efforts addressing the needs of these populations).

"In this environment where TB prevention has been lagging behind... having someone like IMPAACT4TB promoting uptake of this paediatric formulation... has really been instrumental." (Global stakeholder)

By April 2025, GDF reported that 23,000 treatment courses had been delivered to three countries, with an additional 28,400 courses pending delivery to three more countries. Unitaid also reports 1.9 million doses have been procured through domestic sources (India, Nigeria) and the Global Fund. Production issues continue to affect product availability however, with delayed shipments reported as recently as April 2026.

Our conclusion based on the evaluation evidence is that the I4TB investment and range of complementary actions by partners has done well to bring to market a clear improvement for TPT. **The work under this project as well as the direct market shaping work of Unitaid is a clear demonstration of its pathfinding, investing and influencing role in the global architecture and product markets.** However the nature of the market is such that further work needs to continue to develop new and better TPT options including ongoing development of Bedaquiline-based TPT options (as suggested in some consultations). The Unitaid portfolio has had a longer term view with its investments in the Longevity grant aimed at the development of a long-acting injectable formulation of TPT to further improve adherence and delivery. We also view that there is a need to better harness the 3HP/1HP market through further demand side work on accessing household contacts and while the project may well have delivered to its target populations (PLHIV and children) the work cannot be assumed to stop there given availability of the improved TPT option and the continued need to reduce TB infections and disease. More on these aspects is discussed below in the demand and adoption analysis.



Market Shaping Learning Brief

This brief summarises key insights from the I4TB market-shaping intervention for Unitaid, including the contributions of key stakeholders, including direct Unitaid engagement. The analysis draws on stakeholder interviews and document review. Several limitations should be noted. First, the time elapsed since the I4TB investment was designed and the subsequent market-shaping negotiations may have affected stakeholder recall. Second, documentary evidence for some aspects of the intervention was limited or unavailable. Third, some stakeholders who were closely involved in the early stages of market shaping were not available to participate in the evaluation. Where stakeholder perspectives differed on specific events, contributions or decisions, these differences are noted where relevant. Appendix G lists all market shaping tools applied in I4TB and their appropriateness.

³¹ Holt, E. (2024). Child friendly rifapentine formulation is a game changer. Lancet. (24: e84).

I. Complexity of market shaping in a dynamic landscape with multiple partners

The contribution of the I4TB project to developments in the 3HP and 1HP market needs to be understood in light of the following:

- i. **The supply side evolved as a result of the action of multiple players including Unitaid.** Engaged partners included I4TB grantees, Unitaid's direct engagement with suppliers and funders, funders including PEPFAR and the Global Fund, MedAccess, procurement agents including iPlus solutions and GDF, amongst others. In particular, unlike some other Unitaid investments, Unitaid itself played a key role in market shaping alongside the I4TB grantees. As such, I4TB's role was contributory alongside that of many other actors including Unitaid. These partners established and provided the coordination platform for rifapentine-based TPT market shaping and together with Unitaid supported market shaping of rifapentine-based TPT.
- ii. The supply side did not function in isolation and was heavily impacted by developments on the demand side – some of which I4TB directly influenced. The underlying context was shaped by developments in the WHO policy landscape and in UN global commitments and targets. In particular: (i) Evolution of the WHO normative guidelines (underpinned by the I4TB DOLPHIN trials evidence) and the 2018 UN High Level Meeting TPT targets by 2022³² - both of which encouraged country demand and adoption; and (ii) Availability of funding from different global health funders. The supply response had to take place in tandem with these demand-side developments, creating challenges and requiring adjustments along the way.

II. Market shaping instruments and their significance

The choice of an adjustable purchase order (APO) for Unitaid's agreement with Sanofi in place of other market shaping instruments, offered significant advantages:

- i. It avoided extensive documentation and legalities and reduced complexities for the arrangement, which was preferred by engaged actors;
- ii. Was de-risking to the supplier whilst not locking in all of Unitaid's market shaping budget. A direct buy-down arrangement had been considered, but this was deemed to be more expensive. The APO allowed different partners' procurements to count against the agreed volume which was ultimately cost-saving to Unitaid. Savings from the US\$ 20m market shaping budget could later be applied towards market interventions with the generic manufacturers Macleods and Lupin. (*"... if Unitaid were to underwrite a buy down, they would need to reserve the full project budget in a separate pool and they couldn't do anything further with it."* – Global stakeholder).
- iii. The VG by MedAccess was considered by one stakeholder to complement Unitaid's ability to de-risk new markets where Unitaid acts a 'first mover'. The VG came in after initial market confidence and lower ceiling price were established and provided a longer term guarantee to manufacturers. The complexity of rifapentine production and small pool of manufacturers involved was also considered a factor in the added value of a VG-type intervention.

A few stakeholders noted some criticisms of the initial Unitaid and I4TB market approach. Key points raised and an assessment of their validity are as follows:

- *'A better approach would have been to encourage faster introduction of FDCs'* – however consultations with an FDC supplier indicates it would not have been realistic to accelerate the time to obtain WHO PQ and that generics came to market as soon as feasible. It is also noted that Unitaid pushed for the FDC formulation in the TPP later on.
- *'Stockpiling to prevent local supply shortfall was also indicated as an alternate approach'* However, several stakeholders have argued against the validity of this approach given the work done towards procurement coordination to ensure supply was sent based on country readiness.
- *'The US\$15 price point was contested by some as creating perverse incentives for Sanofi to reduce the price further'* - A few stakeholders interviewed considered that as the price of 3HP has fallen further to now under US\$10 per adult course without a proportionate increase in magnitude of demand, this could indicate the initial price ceiling could potentially have been lower. While the appropriateness of the US\$15 price point is beyond the scope of this evaluation, we understand that Unitaid and CHAI had

carefully conducted cost of goods sold analysis and confirmed that this was a reasonable price ceiling to impose at that time. Further this does not adequately account for the more limited demand visibility in 2018-2019 and market uncertainty, with country demand becoming much clearer in the later years of I4TB which also invested significantly in country demand and adoption. Indeed subsequent price reductions were only possible because of the substantial de-risking work of Unitaid and I4TB.

While several challenges were experienced in the supply situation, **overall it appears that the most effective and appropriate market shaping solutions were proposed at each stage with the available information and foresight.** Concluding insights on this topic are as follows:

- Mechanisms for supply-side market shaping need to be adapted to the specific needs. Formulaic volume guarantees for example need not always be applied and other options and differential terms should be actively considered. For example, VGs can reduce prices while preserving more flexibility than a buy-down structure.
- There are pros and cons of providing a reference price to manufacturers – although direct communication of price can also lead to greater market certainty and correspondingly faster action by suppliers, as seen for 3HP.
- Today, a more constrained funding environment suggests previous market shaping tools risk not working as smoothly given more limited donor funding for pooled procurement. While the shift towards domestic financing implies market shaping should look to regional or sub-regional pooled approaches, other sources of up-front financing or other means of stimulating manufacturer confidence and/or offsetting their early investment need to be developed.

The use of the EMAV³³ for pediatric-friendly 3HP was considered as a best practice and “game changer” in catalysing market entry and country uptake of a new product, particularly given dispersible formulations are more costly to produce. The EMAV committed to procure 85,000 tablets, with access conditions including that the 150mg rifapentine child-friendly formulation was available at no higher than the US\$15 per adult 3HP course, meaning that for the first time market entry of a pediatric formulation was more affordable than current alternatives for children and on-par with the adult formulation. While overall there are limited stakeholder perspectives on the suitability of the EMAV in I4TB, with most stakeholders more familiar with I4TB’s initial market shaping for adult formulations, country demand for the pediatric formulation suggests this was an effective instrument. Demand and adoption investments through I4TB were also important in helping to disseminate WHO guidance on pediatric TPT to country stakeholders to encourage orders being placed.

III. Mitigating single supplier risks

Stakeholders familiar with the process identified several key **enablers** that contributed to the successful design and operationalisation of the early market-shaping intervention. These were also informed from previous experience working with Sanofi in terms of the value of a single line of communication with the supplier, alongside improved communication with country programmes.

- i. **Strong stakeholder engagement** throughout, including an “activation meeting” that reviewed each term of the Sanofi deal with partners including PEPFAR and Global Fund.
- ii. **Decision to centralise procurement**, which was operationalised through iPlus solutions (the Global Fund procurement agent) to provide clear visibility on orders and countries. This proved to be critical in the initial year of the Sanofi agreement when demand exceeded supply. iPlus solutions was regarded as a strong partner in coordinating supply and country readiness (*... “readiness coordination was being managed and iPlus solutions also did an excellent job there.”* – Global stakeholder).

³² The 2018 UN High Level Meeting on Tuberculosis set targets for at least 30 million people to have initiated TPT between 2018-2022 (6 million PLHIV and 24 million household contacts, including 4 million children under 5).

³³ Osigbesan, A. et al (2024). The early market access vehicle – An innovative demand-driven model to catalyse introduction of new optimal health products in low- and middle-income countries. Health Policy Open 8. <https://doi.org/10.1016/j.hopen.2024.100135>

- iii. A **market coordination function**, leveraging the existing ARV working group for 3HP, to work with iPlus solutions and key partners to manage supply.

IV. Working with manufacturers

Supply side market shaping is a complex and “non-linear” process, with considerable uncertainty on outcomes and results. Insights on working with manufacturers include:

- i. Generic market entry has considerable risks and timelines should be realistic. This is particularly the case for rifamycin, as API production is complex, energy-intensive, and environmentally challenging, and there are few API suppliers.
- ii. Where large demand is anticipated, support at least two generic suppliers in parallel rather than relying too heavily on one early entrant. Uncertainty of market evolution means that opting to spread one’s risks through multiple options is a healthy approach.
- iii. Volume guarantees for second market entrant should also be carefully considered – particularly in the more constrained donor and health financing context.
- iv. Supplier projections for new product scale-up are often too optimistic. Supply projections can be unreliable; projected manufacturing capacity may not translate into actual production.
- v. There is real value in supporting generics with the WHO prequalification process which can be complex and high cost for these suppliers. Flexible approaches can be adopted, such as providing additional quality assurance capacity to generics (as by FHI 360 under I4TB).
- vi. Future supplier support strategies should include at least one regional or local manufacturer, potentially through tech transfer. In 2025 I4TB provided funding to CPT Pharma in South Africa to diversify API production capacity. This followed the termination of USAID funding to CPT funding due to the 2025 USAID Stop-Work Order (see the Sustainability section 2.2.3 for more details).

V. Importance of demand creation and tight alignment with supply

A strength of I4TB was its country-focused demand creation, which engaged with national stakeholders, civil society and community partners to create an enabling environment for 3HP (refer to the CCSE learning brief). There are several insights concerning the linkage between supply and demand from I4TB as follows:

- i. Demand creation and supply security need to be much more tightly aligned; otherwise shortages damage confidence and later demand.
- ii. From the perspective of communities and health stakeholders, 3HP was starting “from a deficit” based on negative experiences with long monotherapies. Impurities raised the stakes further, with some countries having to destroy 3HP products. CCSE activities under I4TB were valuable for overcoming this ‘deficit’ and providing clear messaging on supply quality issues. These lessons are likely to remain highly relevant for future product introduction in contexts where public confidence in health innovations is weak, or for other TB prevention innovations.

VI. General insights on partner coordination

- i. Coordinated supplier engagement by global health partners is critical to ensuring supplier confidence and faster action. Market shaping requires tight coordination across donors, procurement agents and manufacturers; fragmented signalling weakened negotiations.
- ii. The I4TB ARV procurement working group model of 3HP procurement coordination is a best practice model offering good insights on organisation coordination and managing demand and supply interface.
- iii. An independent coordination mechanism can improve allocation fairness, reduce fragmented messaging to suppliers, and align procurement with programme readiness.

2.2.2. Demand and adoption

1b. Demand and adoption. How effective were the projects in generating evidence to inform WHO guidelines on rifapentine-based therapies for household contacts under two years and HIV-positive pregnant women? To what extent did it support the adoption of rifapentine-based TPT in project countries and beyond? What has been the effect of the CBO / CSO advocacy on uptake of TPT tools?

Assessment of I4TB's effectiveness on demand and adoption of rifapentine-based TPT regimens focuses on evidence generation and influence on guidelines and policy (global and national level), direct and catalytic impact of I4TB in terms of product uptake across the 12 project countries and beyond, as well as the contribution and effectiveness of community and civil society-led efforts. Catalytic impact following project close in 2022 in I4TB countries and beyond is covered as part of the scalability assessment (Section 2.3).

Finding 4. Evidence generated through I4TB was highly influential, filling critical evidence gaps on TPT for children and generating important data and implementation lessons that informed WHO guidance as well as national contact investigation and TPT policies.

Strength of evidence	Rationale
 High	Strong consensus from consultations, supported by documentary evidence on I4TB's contribution to informing WHO policy and country adoption of rifapentine-based TPT. DOLPHIN-Moms and DOLPHIN-Kids studies are not yet published, but findings show positive results and consultations suggest they will influence global TPT policies for pregnant women and children living with HIV later in 2026.

"These studies were the key ones informing policies...and government decisions. And the WHO endorsement was key" ... "The Aurum-led consortium has been the go-to group for accessing evidence on TPT". (Global stakeholder)

In addition to the DOPHIN studies described above, I4TB-supported studies focused on paediatric TB filled critical evidence gaps regarding effective TPT regimens for children (i) with and without HIV (TBTC Study 35, DOLPHIN Kids); (ii) exposed to both DS-TB (TBTC Study 35), and (iii) DR-TB (TB CHAMP). The results of this research, along with operational studies undertaken by the Unitaid CaP-TB investment, have yielded important data for WHO guidelines and national level contact investigation guidelines. Unitaid Enabler support added value particularly in the WHO guideline development process (Box 2 describes complementarity in Unitaid's TB prevention research).

At the global level, stakeholders mentioned the importance of I4TB's influence on WHO guidelines as a key step to ensure rapid uptake of 3HP at country level. One stakeholder referred to the I4TB consortium as a "hub of knowledge" that WHO continued to draw on to inform operational guidelines, practical tools and capacity building.

Figure 2.4 summaries the key evidence generated by I4TB and the policy implications. In total, approximately nine WHO policies and guidelines were significantly or in-part informed by work under I4TB to date, including the foundational WHO TPT 2018 and 2020 guideline expansion for 3HP on PLHIV taking DTG, as well as the WHO TPT 2024 guidelines on pediatric dosing, and the 2025 HIV treatment guidelines (Appendix E lists key I4TB studies and analysis and implicated WHO policies). Among the many evidence-generation achievements, stakeholders pointed to the following as particularly significant and value-adding, with further detail in the box below:

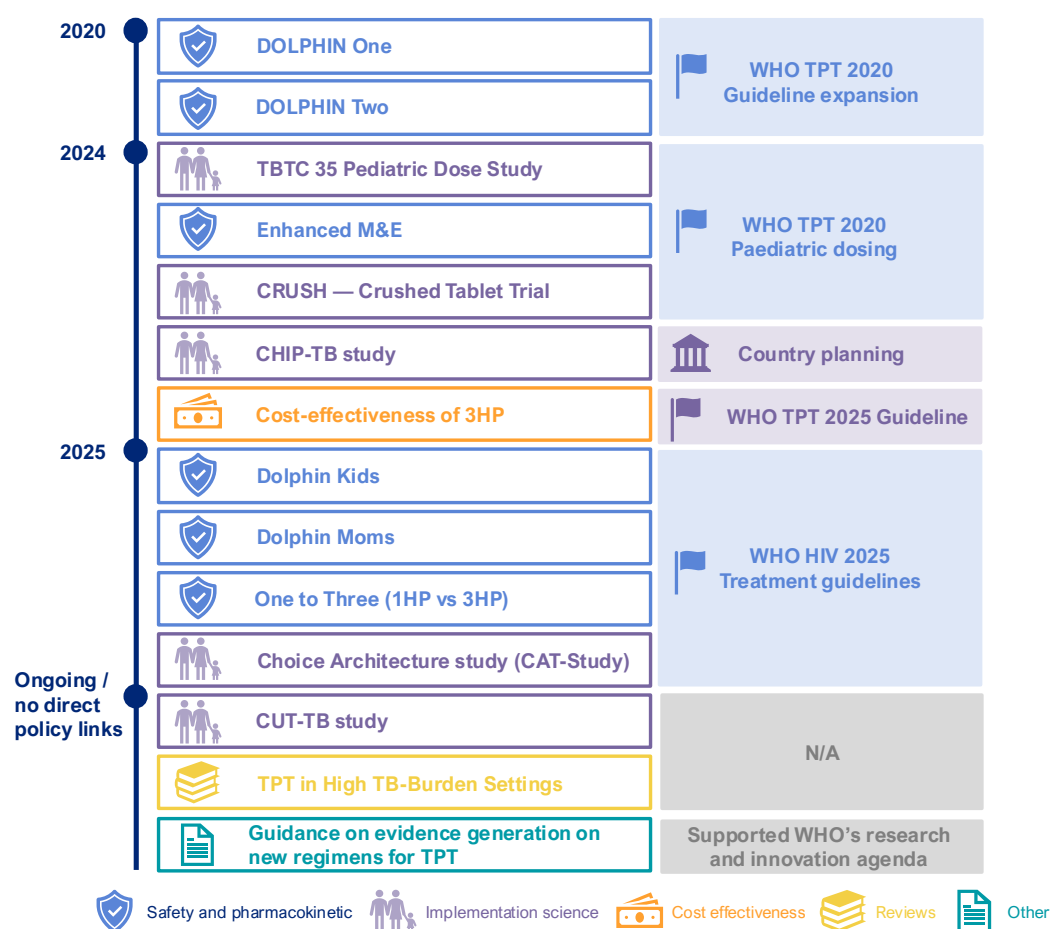
- **Safety and effectiveness of 3HP for PLHIV (2017-2019):** Unitaid's support for the DOLPHIN and DOLPHIN TOO pharmacokinetic studies in South Africa provided evidence to support the use of 3HP for among adult PLHIV on dolutegravir-based ART (as described in Finding 1).
- **Dose-finding and safety of 3HP for children under 2 years (2019-2024):** I4TB provided strategic funding to expand the TB Trials Consortium (TBTC) Study35 to include sites in South Africa and increase the sample

size of children under two years old.³⁴ This provided data to support the use of rifapentine-based TPT among very young children (< 2 years) which had been missing. One consultee noted that Unitaids's flexible use of funding in expanding an existing study to address an evidence gap represented a unique value-add, as other funders lacked this level of flexibility. Study results have informed the ongoing DOLPHIN KIDS study (see below).

- 3HP for pregnant women, children and adolescents living with HIV (2023-ongoing):** Under the I4TB costed extension, pharmacokinetic studies of 3HP and dolutegravir in pregnant women, children and adolescents living with HIV are underway through the DOLPHIN Kids (initiated May 2023) and DOLPHIN Moms (initiated January 2024) studies in South Africa. Final WHO recommendations for the use of 3HP for these two populations will be informed by the results of these studies and are expected to be released as updates to the TPT operational handbook, and to a lesser extent, changes in the text of the TPT guidelines, by the end of 2026. Findings were presented at the 2026 Conference on Retroviruses and Opportunities Infections (CROI) showing 3HP and dolutegravir are also safe to use together in children living with HIV and in pregnant persons with good adherence support.

Though these I4TB studies and others, including operational research such as CHIP-TB, have been influential, there were reports of delays in WHO Research Ethics Review Committee (ERC) approval for I4TB studies which affected timely initiation during the project period (the most significant example cited was a delay of 9 months to 1 year).

Figure 2.4: Summary of key evidence generated by I4TB



³⁴ Study 35 provided data on the safety, tolerability, and appropriate dose of 3HP in the youngest children (< 2 years) in South Africa and the US. Liu W, et al. (2025). Pharmacokinetics and safety of rifapentine in children: dosing for latent tuberculosis infection. J Antimicrob Chemother. Apr 2;80(4). DOI: 10.1093/jac/dkaf029



Box 2. Complementarity to other Unitaids TB prevention evidence generation and Enabler support

In addition to I4TB, Unitaids funded two projects focused on **TB prevention for children and household contacts**, yielding complementary evidence to inform TPT for children:

- **Benefit Kids** (2019-2024) implemented the TB CHAMP study, which filled an evidence gap on the use of levofloxacin for TPT among child contacts of **DR-TB cases**. The results were presented at the World Lung Health Conference in 2023. WHO now includes a recommendation for using a six-month regimen of levofloxacin for children under 15 years old who are close contacts of an individual with DR-TB. The 2025 Global TB Report notes that 49 countries have already begun to use this regimen, including India, Mozambique and South Africa among I4TB focus countries
- **CaP-TB** (2019-2022) was a multi-country project led by EGPAF that implemented different models of household contact investigation with a focus on identifying promising ways to reach child contacts and deliver the 3HR TPT regimen.³⁵ Results from this project were used to inform WHO's 2022 operational guidelines on the management of TB in children and provided practical case studies on how to implement contact investigation in a variety of settings.³⁶

Together, Unitaids support to TBCT Study³⁵, DOLPHIN-Kids and TB CHAMP studies filled critical evidence gaps regarding effective TPT regimens for children (with and without HIV) exposed to both DS-TB and DR-TB, and jointly with CaP-TB have yielded important data and lessons that informed WHO guidelines and national level contact investigation guidelines.

Through the **WHO enabler grant**, I4TB has played a key role in translating evidence into policy, primarily through the WHO guideline development process:

- The WHO guidelines for TPT regimens have been updated multiple times from 2018 to 2024, utilizing the results of Unitaids-supported research and the resources provided by I4TB to support the guideline development process itself.
- Supported the development and publication of [Guidance on evidence generation for new regimens for TPT³⁷](#), which consolidated lessons learned from the research supported by I4TB and other TPT trials. This publication provides a detailed overview of WHO processes such as prequalification of regimens and guideline development groups, along with practical examples of successful trials and best practices for the design and implementation of TPT research.
- Supported WHO regional dissemination workshops on the 2024 TPT guidelines and Paediatric drug optimization exercises for TB (PADO-TB) meetings and reports that are convened to establish priorities for the development of child-friendly formulations of TB medications, including TPT. Unitaids' support for and participation in the PADO-TB process resulted in a decision to recommend a child-friendly formulation of rifapentine instead of an FDC of rifapentine and isoniazid to maintain flexibility in future use of rifapentine among children and maintain a lower cost for rifapentine-based child-friendly formulations (discussed in the Relevance section).

³⁵ The 3HR TPT regimen consists of isoniazid (H) and rifampicin (R), taken every day for 12 weeks (90 doses in total). 3HR is an older WHO-recommended short-course TPT regimen and was already being used before rifapentine-based regimens (3HP/1HP) became available. By comparison the 3HP regimen is taken once a week for 12 weeks for a lower total dose (12 doses total).

³⁶ WHO (2022). WHO operational handbook on tuberculosis: module 5: management of tuberculosis in children and adolescents.

³⁷ WHO (2025). Guidance on evidence generation on new regimens for tuberculosis preventive treatment. Available at: <https://tbksp.who.int/en/node/3187>

Finding 5: I4TB successfully catalysed uptake of 3HP for PLHIV and child contacts. It was less successful in adoption of TPT for adult household contacts due to lower prioritisation at the policy level, and delivery and financing constraints.

Strength of evidence	Rationale
 High	Strong consensus from consultations, supported by documentary evidence on I4TB's contribution to country demand and adoption of 3HP, noting other partners including PEPFAR had also influenced 3HP use for PLHIV in PEPFAR-supported countries. Strong evidence of less progress in 3HP or 1HP uptake for household contacts during the I4TB project period.

“The impacts of [I4TB] cannot be underestimated. It has shaped and made possible the very rapid uptake of 3HP. And nowadays, if you come to [these] countries, people talk about 3HP as if it's just normal. As if it's nothing special, which is, of course, good but then you forget it's only been a few years.” (I4TB implementing partner)

I4TB initially supported uptake of 3HP in 12 focus countries through direct support to Ministries of Health, National TB Programs and National HIV/AIDS programs. The project employed national and targeted sub-national engagement to support policy buy-in and demonstrate the feasibility of implementation. It also supported catalytic uptake beyond focused-sites and in non-project countries.

- At national level, the project worked with relevant authorities to register products with pharmaceutical regulatory authorities and forecast quantities needed to provide 3HP to PLHIV and contacts. I4TB also participated in national TPT technical working groups to support the transition to 3HP, for example, in Tanzania, where the government was initially not supportive of 3HP and was persuaded by the recommendations from the working group, which included presentations of results from Unitaids-supported research (e.g., DOLPHIN studies) and insights from the introduction of 3HP in other I4TB focus countries. Working with National TB Programs and technical partners, I4TB provided training for health care providers on implementing of new guidelines and leveraged this capacity building to address misinformation about TPT and disseminate accurate information on the benefits and risks.
- At subnational level, I4TB provided intensive support to selected target sites to train providers on 3HP distribution and monitoring. Notably, the project utilized existing DHIS2 reporting systems to capture data on the initial rollout at sites, adding only the bare minimum of additional data elements to monitor uptake by priority populations (e.g. PLHIV newly enrolled on ART, PLHIV stable on ART, household contacts and in some cases, by age group). By the end of country-focused I4TB implementation in December 2022, target sites across the 12 project countries had reported initiating 3HP for 123,700 people living with HIV (PLHIV) and 12,142 household contacts. This was lower than planned/ targeted but Aurum reported that implementation was affected by several challenges, including COVID-19-related delays, nitrosamine impurity concerns, and supply constraints.
- Despite these constraints, 3HP initiation expanded beyond the I4TB target sites to “catalytic” sites in project countries, driven by governments and other country partners, reaching over 504,000 PLHIV and nearly 45,000 household contacts by the end of 2022 (Figure 2.5, Figure 2.6).

Figure 2.5: Total 3HP uptake by end 2022 – PLHIV in I4TB countries

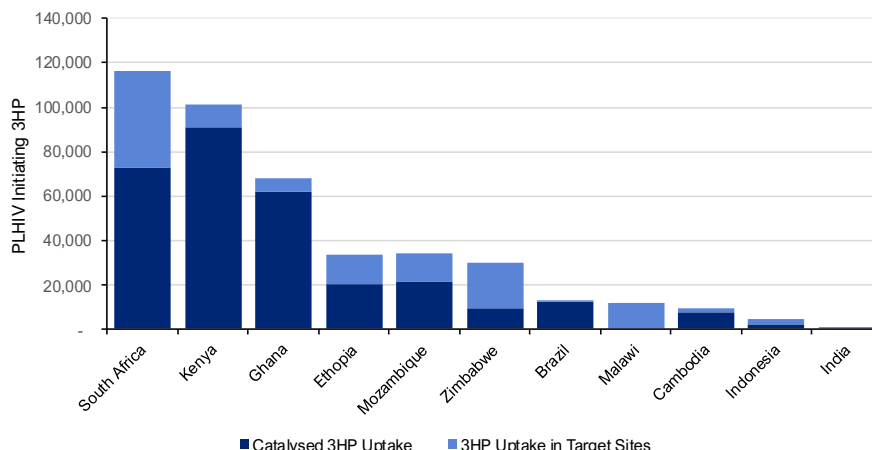
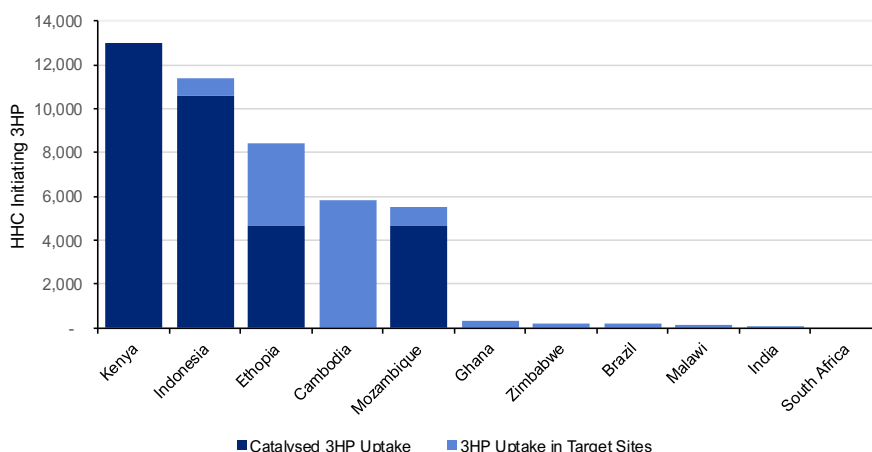


Figure 2.6: Total 3HP uptake until 2022 – Household contacts I4TB countries³⁸



- I4TB also conducted several operational studies to **guide decision-making on optimal delivery models in different contexts**. Key studies were the CHIP-TB study (Ethiopia and South Africa) comparing household and community-based strategies to provide 3HP to child contacts and a choice architecture study in Malawi, Mozambique and Zimbabwe to explore clinical decision-making among TPT prescribers.
- **I4TB catalytic impact extended beyond the 12 project countries through responding to multiple country requests to procure rifapentine-based TPT, including Pakistan and Sierra Leone.** Aurum's reputation as a 'go to' organisation for introduction of 3HP was reported to have spurred requests for support from Sierra Leone, Thailand, and Pakistan related to 3HP forecasting and procurement and planning for 3HP introduction.

The key factors influencing uptake (in I4TB target sites and catalytic) were (i) varying timelines for registration of generic rifapentine with regulatory authorities and TPT guidelines; and (ii) opportunity to integrate TPT into existing HIV services, which drove high initiation among PLHIV. In contrast, initiation among household contacts was challenged by lack of routine contact investigation.

³⁸ Based on Aurum 2024 project reporting. Not all countries provided data.

- The countries demonstrating the greatest catalytic impact on TPT initiations among PLHIV were, in order, Kenya, Zimbabwe, Kenya, and South Africa (Figure 2.5). For household contacts, Kenya showed the greatest catalytic impact, followed by Indonesia, Ethiopia, and Mozambique (Figure 2.6). Kenya, South Africa, and Zimbabwe each reported more than 100,000 3HP initiations by the end of 2022 (see Box 3).



Box 3. Kenya reported the largest 3HP catalytic scale overall among I4TB countries. Key enablers reported by Aurum³⁹ were:

- **Early policy and regulatory readiness.** Kenya was one of the first I4TB countries to include rifapentine on its essential medicines list, which was released in 2023.
- **TPT rollout among PLHIV had already started before 3HP scale-up.** Kenya had been rolling out TPT among PLHIV as early as 2017, so 3HP was introduced into an existing delivery platform rather than starting from scratch.
- **Multiple procurement channels.** From 2020, Kenya had access to 3HP through several routes, including PEPFAR, CHAI/Unitaid and the Kenya MoH, reducing reliance on a single funder or supply source.
- **Stronger TB and HIV reporting systems.** CHAI supported the development of an electronic order management platform linking KHIS, Kenya's national reporting tool, with KEMSA's logistics management information system. This was seen as supporting efficient roll out.

- Uptake was considerably lower in Asian countries and Brazil, where between 500 and 15,000 individuals initiated 3HP by 2022. Reported reasons for lower uptake in some countries included provider hesitancy and limited confidence in prescribing TPT, as well as supply chain challenges at both national and subnational levels. Slow uptake in India was reportedly due to India having its own regulatory processes, and significant progress has since been reported (refer to Box 4, Box 6 and Scalability findings). One global stakeholder also noted that some countries were slower to transition to 3HP because they prioritised depletion of existing isoniazid monotherapy stocks (for 6H/9H regimens) before introducing newer regimens. As these legacy stocks are exhausted, uptake of 3HP is expected to accelerate further in the coming years.



Box 4. Contributions of I4TB in Zimbabwe and India

I4TB support in Zimbabwe illustrates how the project supported adoption and demand creation for 3HP among PLHIV from procurement, policy, technical assistance and advocacy perspectives. Beyond the initial donation of 95,100 rounds of TPT, I4TB contributed to new TPT guidelines and capacity building for 3HP implementation at site level in collaboration with the Ministry of Health and Child Care (MoHCC). Additionally, evidence and lessons learned from early 3HP implementation shaped the National Tuberculosis and Leprosy Programme Strategic Plan (2021-2025) and informed the TPT sections of the 2023 National TB and Leprosy Management Guidelines. Civil society partners trained "expert clients" to provide testimonials about their experience taking 3HP through existing peer support groups for PLHIV and trained community health workers on treatment literacy approaches to support demand creation.

"The initial procurement for the 20 sites was done under IMPAACT4TB. Usually, there are teething problems when a new product is being introduced, but now there was already a pathway from the pilot of the 20 sites, so everything moved on well." (Zimbabwe stakeholder)

I4TB has been catalytic in India by providing in-country demonstration of 3HP at a time when adult latent TB guidelines were not yet in place and by keeping rifapentine-based TPT active in national policy discussions. The work came at a "critical juncture" when India had no latent TB guidance for adults and practice was limited mainly to PLHIV and children under five. The project also helped keep 3HP visible during debates on drug interactions, introduction, and impurity concerns, and gave national technical bodies something concrete to follow in India. The project generated local

³⁹ Aurum (2022). Kenya close out country report

evidence, which was important because national bodies preferred to see evidence generated in India rather than relying only on international trials. This contributed to a policy update as the 2021 Guidelines for Programmatic Management of TB Preventive Treatment aligned with WHO's 2020 consolidated TPT guidance and recommended introduction of shorter TPT.⁴⁰

Strong integration with HIV platforms, and lower uptake among household contacts including children

- PLHIV constituted the greatest share of 3HP uptake by population group (92% of the over 684k initiations credited to I4TB). Stakeholders view this was strongly driven by country commitments to UN High Level Meeting TPT targets by 2022⁴¹ with significant support from PEPFAR and the Global Fund. This also reflects the strong integration and leveraging of PEPFAR investments in HIV care and treatment services.
- In focus countries, significantly lower uptake among household contacts was also attributed to the fact that contact investigation had not yet been established as a routine practice at sufficient scale (*"The need might be there, but the demand is not there... because programs aren't doing household contact tracing"*). In Ethiopia, which had the third highest number of total household contact initiations (~8,000), the presence of the aforementioned Unitaid CHIP-TB study may have contributed to higher uptake by generating lessons and evidence that strengthened contact investigation planning and implementation. One global stakeholder also noted that, in settings where countries are hesitant to offer 3HP to young children due to the absence of global guidance on dosing and appropriate formulations, households may be less likely to initiate TPT for other eligible household members as well.
- Despite I4TB's inclusion of children and pregnant women in key research studies, uptake among these populations at country level remained sub-optimal during the project period. This finding is not unexpected given low contact tracing overall, and that a child-friendly 3HP formulation only became available through Unitaid's EMAV in early 2024, relatively late in the project implementation period, and many countries had not yet established the policies, guidance, or implementation experience needed for widespread use. Additionally, there have been delays in delivery and quality assurance challenges. In Indonesia, as the paediatric formulation has a shorter shelf life, Aurum reported the government was hesitant to place an order until the country was ready to implement, so as to minimize the risk of expiry.⁴² One global stakeholder also noted that, where countries are hesitant to offer 3HP to children in the absence of global guidance on dosing and appropriate products, households may be less likely to initiate TPT for other eligible household members as well.

Finding 6. Collaboration with civil society and community-based organisations was a key contributor to I4TB's success in generating demand for and adoption of 3HP. These organisations played a critical role as trusted messengers, helping to dispel misconceptions about TPT and communicating the benefits.

Strength of evidence	Rationale
 High	Strong consensus from consultations, supported by documentary evidence on the value-add of I4TB CCSE

⁴⁰ National TB Elimination Programme Central TB Division, Ministry of Health & Family Welfare, Government of India, (2021), Guidelines for Programmatic Management of Tuberculosis Preventive Treatment in India.

⁴¹ The 2018 UN High Level Meeting on Tuberculosis set targets for at least 30 million people to have initiated TPT between 2018-2022 (6 million PLHIV and 24 million household contacts, including 4 million children under 5).

⁴² I4TB CSO Success Stories. Champions of TB Prevention Real Stories, Proven Strategies. Available at: <https://impaact4tb.org/wp-content/uploads/2025/12/IMPAACT4TB-CSO-Success-Stories-R6-3.pdf>

I4TB employed three broad demand creation strategies: (i) developing significant advocacy and communication materials that were adapted at country level to support demand creation at community level; (ii) training on advocacy and treatment literacy for affected communities and providers to address misinformation and improve attitudes towards TPT; and (iii) partnering with Treatment Action Group (TAG) to implement a capacity building and small grants program to support local organizations. More details are provided in the CCSE learning brief at the end of this section.

The small grant program overseen by TAG made resources and training available to 22 CSOs and CBOs in 11 countries to design, implement and monitor innovative advocacy activities. These one-time grants piloted innovative efforts to reach specific priority populations who could benefit from TB prevention services (Box 5). Given the long history of TPT and associated challenges in affected countries, TAG also worked through CSOs, CBOs and relevant provider networks and associations to address misinformation about TPT and promote its use among PLHIV and household contacts



Box 5. I4TB supported locally-driven approaches to reach otherwise neglected populations for TPT.

In **Indonesia**, PETA (Pejuang Tangguh/Strong Fighters) identified pregnant women as a population often left out of TB prevention efforts and adapted existing local communication materials to convey messages about the importance of TB screening and prevention. After first attempting to work with private midwives, PETA realized they were likely to have more success collaborating with primary health care centres (*puskesmas*) to reach women through established prenatal support groups. This experience highlights the importance of working with trusted messengers to bring information about TPT to a specific population who may be difficult to reach.

In **India**, the Global Coalition of TB Advocates (GCTA) engaged populations which had never been included in TPT, for instance working with LGBTQ+ organisations and organisations working with injection drug users to enhance TPT treatment literacy and provide training on how to undertake advocacy for TPT. *“For the first time, national TB prevention conversations included LGBTQ+ advocates, alongside PLHIV networks, drug user forums, and people affected by TB.”*⁴³

Civil society and community-based organizations were critical to the success of I4TB at country level through ensuring that local priorities and potential barriers to adoption of 3HP were addressed. These partners helped build and maintain momentum for scale up of 3HP through multiple channels in project countries. In some countries, CSOs and CBOs were challenged by previous negative experiences with isoniazid monotherapy and associated health provider concerns on risk of isoniazid resistance; they were not only working to educate stakeholders about the benefits of 3HP but were also faced with a legacy of side effects and long regimens that were not always implemented consistently in focus countries. Community advocates shifted the narrative on TPT to promote the shorter regimens with FDCs that are easier to take and have fewer side effects.

“TB preventive treatment was starting, not from zero, but from a deficit, when it came to community acceptability... being able to offer something different, that was shorter and looked really different, was helpful.” (Global stakeholder)

The importance of I4TB’s collaboration with trusted CSO and CBO partners is also illustrated by the project’s response to concerns about nitrosamine contamination. This was exemplified in Malawi, where a batch of 3HP was recalled after delivery in country. The Coalition of Women Living with HIV/AIDS (COWLHA), a women-led, longstanding organization, was mobilized to reassure providers and PLHIV that 3HP was safe and to support the Ministry of Health in communicating the actions taken to remove and replace contaminated batches. TAG developed informative but easy to understand materials, including FAQs, that were adapted for use in the country. COWLHA staff met with health care workers to provide timely, accurate information about the contamination and recall, and

⁴³ I4TB CSO Success Stories. Champions of TB Prevention Real Stories, Proven Strategies. Available at: <https://impaact4tb.org/wp-content/uploads/2025/12/IMPAACT4TB-CSO-Success-Stories-R6-3.pdf>

used local radio and Q&A sessions in affected facilities to address concerns and maintain trust in TB prevention services. (“What could have been, like, a huge setback in public kind of messaging crisis really wasn’t... and for me, it illustrated the value of having community work go alongside the market work.” - CSO stakeholder).



CCSE Learning Brief

Although relatively small in financial terms (approximately US\$1 million for the small grants programme, in addition to TAG’s consortium budget for coordination and capacity strengthening), CCSE was an integral component of I4TB’s overall strategy and widely viewed by stakeholders as critical to successful introduction and uptake of rifapentine-based TPT. While Unitaids’ approach to CCSE has evolved considerably since I4TB, these lessons remain relevant.

I. Contribution of CCSE for 3HP introduction

Patient literacy and overcoming negative perceptions of TPT: At the start of I4TB, provider and patient perceptions of TPT were often negative due to the long duration and side effects associated with 6H regimens. Introducing shorter rifapentine-based regimens therefore required more than improved supply and pricing; it also required trusted intermediaries capable of building confidence, addressing misconceptions, and translating global policy shifts into local acceptance and demand. Civil society and community-based organisations played this role effectively, bringing credibility and community trust that government and technical actors alone could not achieve.

Key contributions of the CCSE component included:

- Investment in trusted community actors, including women-led organisations, religious leaders, provider associations, and organisations representing affected populations, to support demand generation at national, community, facility, and household levels.
- Capacity strengthening for local partners in areas such as treatment literacy, intellectual property, communications, community-led monitoring, and data use.
- A small grants mechanism that enabled CSOs and CBOs to pilot locally adapted approaches to stakeholder engagement and 3HP uptake.
- Stakeholders highlighted several products developed under I4TB, including *An Activist’s Guide to Rifapentine TB Preventive Treatment*, as having value beyond the project and continued global relevance.

II. Engagement of TAG

The selection of TAG as the lead partner for CCSE was viewed as strategically advantageous. Through USAID funding, TAG was already supporting local NGOs and had existing experience introducing TB innovations and strengthening advocacy capacity. This provided a strong platform for rapidly identifying capable local partners and tailoring engagement strategies to country context. In several countries, TAG leveraged existing relationships to support advocacy training, treatment literacy, and communication activities related to 3HP introduction.

III. Challenges and lessons

Managing CSO engagement

The timing and intensity of civil society engagement varied considerably across countries. Some stakeholders reported that CSOs were engaged early and meaningfully in policy discussions, while others felt involvement came too late to shape guideline development and early adoption processes. In some contexts, assumptions regarding government–civil society collaboration also proved overly optimistic. One country example demonstrated that direct advocacy by patient groups toward the Ministry of Health generated resistance, with concerns that advocates were being externally influenced. I4TB subsequently adapted its approach by supporting more neutral technical coordination mechanisms to advance dialogue on TPT introduction. Additionally, the small grant program ended earlier than the overall implementation period, so interventions that came later in the project (ex, EMAN for child-friendly formulations) did not benefit from the direct financial and technical support provided to CSOs in the early years of the project.

Capacity strengthening and sustainability challenges

The experience also demonstrated that localisation requires substantial upfront investment in oversight and capacity strengthening. I4TB was implemented during a broader donor transition toward localisation, particularly under USAID's new TB business model announced at the 2018 Hight Level Meeting to shift more implementation funding to local NGOs. This had included managerial and financial capacity building, as many local NGOs did not have experience managing US government funding and fulfilling reporting requirements. TAG reported that supporting newer partners required a highly hands-on management approach and considerable effort during early implementation.

Today, stakeholders note that many of these organisations have since strengthened their institutional and financial management capacities and are now better positioned to manage donor funding more independently. This suggests that Unitaid's investment in local partner capacity generated longer-term value beyond the immediate objectives of I4TB. The 2025 USAID funding cuts, however, pose a significant risk to the sustainability of CCSE efforts in TB prevention. Many implementing partners, including local CSOs and CBOs, were forced to halt or scale back activities, highlighting the vulnerability of community engagement structures that remain heavily donor dependent.

Several stakeholders reported the scale and duration of funding allocated to CCSE underestimated the level of effort required to sustain community engagement and policy influence. The small grants programme represented less than 1% of the total I4TB budget, with average grant sizes of approximately US\$45,000 across 22 organisations. While widely regarded as catalytic, the one-year funding cycle limited sustainability, continuity of advocacy efforts, and long-term relationship building with policymakers and communities.

IV. Implications for Unitaid

These lessons are likely to remain highly relevant for future TB prevention innovations, including TB vaccines and next-generation preventive therapies. Stakeholders emphasised that in contexts where public confidence is weak, or where perceptions begin "from a deficit," as was the case for 3HP, civil society engagement remains essential for building trust, addressing misinformation, and supporting uptake. Since I4TB, Unitaid has substantially strengthened its approach to CCSE through its 2023–2027 Strategy and CCSE framework. The lessons below reinforce this direction and identify opportunities to further strengthen future investments

- Strategies and lessons learnt from I4TB's experience working with CSOs should be incorporated into future projects, including multi-year funding periods for community partners and planning for capacity-building efforts that may be required for local organizations.
- Civil society partners and providers who prescribe TPT and manage service delivery to eligible populations should be at the table early in the design process and meaningfully included in discussions with manufacturers and global TB actors.
- Families and communities should be at the centre of CCSE efforts, and caregivers and young people are specific affected populations whose perspectives should inform CCSE activities.

Demand and adoption: Key lessons and implications for Unitaid

Key strengths

- **Align evidence generation with country priorities and major financing partners.** I4TB successfully anticipated that uptake of 3HP among PLHIV would depend on PEPFAR and WHO endorsement for people receiving DTG-based ART. Early investment in the DOLPHIN studies helped unlock policy support and accelerate scale-up.
- **Invest early in civil society and community engagement and understanding of barriers and enablers to demand.** CSOs and CBOs were essential for rebuilding trust in TPT, strengthening treatment literacy, addressing provider concerns about resistance, and maintaining confidence during supply disruptions and nitrosamine-related issues.
- **Maintain flexible funding mechanisms in Enabler support and projects.** Transparent consortium management and use of realised savings allowed Unitaid to support procurement and introduction of 3HP in

additional countries as demand grew. The WHO Enabler Grant complemented I4TB effectively by supporting rapid WHO guideline review and enabling timely action on emerging evidence.

- **Retain flexibility** to expand support beyond initial target countries.
- **Leverage WHO rapid communications to accelerate country adoption.** Early policy signals through WHO 'rapid communications' generally enabled countries to proceed with implementation ahead of formal guideline updates, including for paediatric dosing recommendations. Still, there was scope for enhanced communication to ensure government awareness of new guidelines.

Areas for improvement

- **Strengthen coordination across related Unitaïd investments.** Projects with overlapping objectives, such as I4TB and CaP-TB, could benefit from more structured mechanisms to share implementation lessons, align country support, and minimize risk of fragmented approaches. The long GAD process for projects is also implicated as Unitaïd then had two projects running concurrently in Ethiopia and South Africa which were focused on different TPT regimens.
- **Coordinate more closely with partners supporting contact investigation and service delivery.** Uptake among household contacts remained constrained in settings where contact investigation systems were weak, particularly in lower HIV burden countries. More coordination with USAID a key investor at the time, may have facilitated I4TB efforts in household contacts.
- **Expand partnerships to better reach underserved populations.** Future TB prevention investments could more systematically engage private sector and workplace-based platforms to improve access for men and other underserved groups at elevated TB risk (similar to the private sector component of HIVST investment).
- **Sequence demand creation more closely with supply readiness, as also flagged above in terms of lessons learn from market shaping.** Some stakeholders felt that rapid demand generation before stable supply was secured created short-term credibility risks during delays and nitrosamine-related disruptions. Future introductions may benefit from stronger forecasting and phased rollout approaches where trust in TPT is already fragile. COVID-19 disruptions, which significantly affected TB programs may also have contributed to early demand-supply imbalance. Noting also that nitrosamine contamination was also a unique project risk which slowed implementation in some countries.

2.3. SCALABILITY, IMPACT AND SUSTAINABILITY

The assessment of scalability begins with the global scale-up of rifapentine-based TPT, followed by an examination of continued scale-up in the 12 I4TB countries after support ended in 2022. Impact and sustainability are assessed alongside scalability, focusing on whether progress has been maintained amid changes in the global health financing landscape, including funding, country demand, and supply security. Sustainability also considers early progress in local API production and I4TB's contribution to strengthening Aurum as a leading TB actor in a high-burden country.

2.3.1. Scalability

2. How have the investments contributed to country and global conditions for scale up?

Finding 7: I4TB made a major contribution to the scale-up of rifapentine-based TPT in project countries and catalysed broader global uptake. Rifapentine-based regimens now account for nearly half of all TPT initiations, though further expansion is needed across priority groups and through increased household contact tracing.

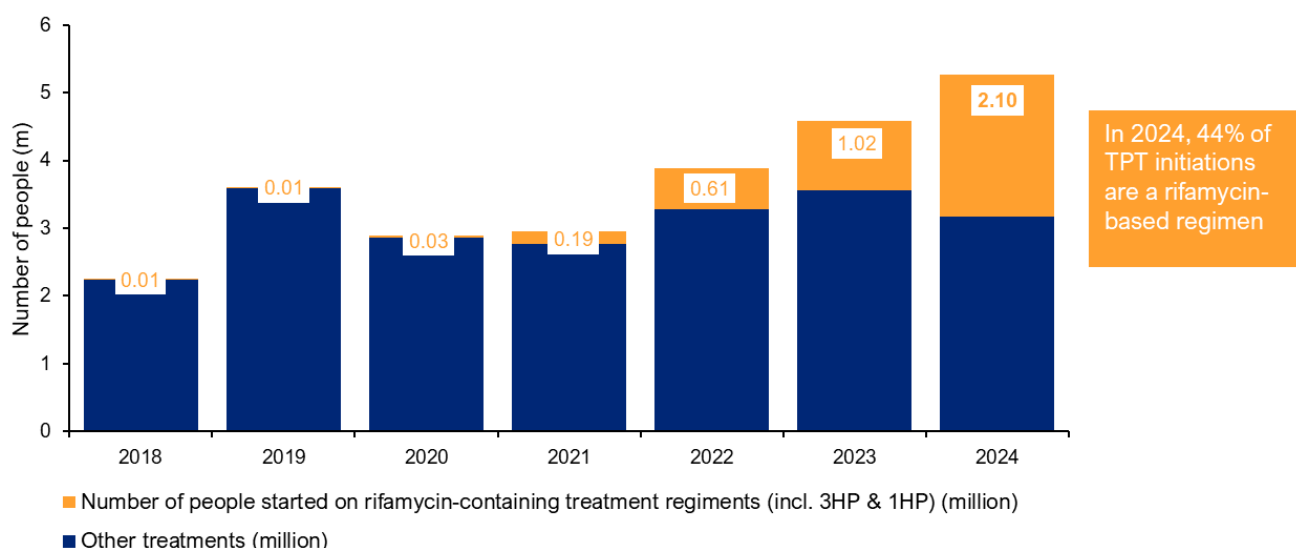
Strength of evidence	Rationale
 High	Strong consensus from global and country level consultations, supported by documentary and data evidence (e.g. Unitaaid scalability framework assessment, WHO data).

At the time I4TB was awarded in 2018, the United States was the only country routinely procuring 3HP for TPT among eligible populations. By the end of the first phase of I4TB in August 2022, 71 countries had begun procuring 3HP, and this has risen to 105 countries as of 2025.

WHO reports the number of people treated using shorter regimens is rising, consistent with the time period of I4TB and catalytic aims. Uptake of shorter TPT regimens (including 1HP and 3HP) as a proportion of TPT increased from less than 1% in 2018 to 44% in 2024 (Figure 2.7). This represents a growth from 0.19 million people in 52 countries in 2021, to 2.1 million people in 88 countries in 2024. Globally, the number of people receiving TPT (long and shorter acting regimens) has increased between 2015 and 2024 from around 1 million to over 5 million.⁴⁴ This increase can be significantly attributed to I4TB catalytic effect. Experts also report that any lag in use of 3HP in countries with high TPT coverage could indicate a preference to first deplete existing isoniazid supply before fully transitioning to 3HP, as observed in Mozambique under I4TB.

⁴⁴ WHO (2025) Global Tuberculosis Report

Figure 2.7: Uptake of rifapentine-based TPT (including 1HP and 3HP) as a proportion of all TPT initiations 2018-2024⁴⁵



TPT scale-up has differed across priority populations over time (Figure 2.8). Among PLHIV and household contacts, key barriers to further scale are identified, including weaknesses in national programs for ruling out active TB disease and swift initiation of TPT:

- People living with HIV:** TPT provision increased steadily from 2015, with a peak of 3 million initiations in 2019, before a gradual step wise decline. According to stakeholders, this reflects the initial strong demand and effort to integrate a single course of 3HP with ART platforms and reach those who had previously not been initiated. The 2022 HLM targets (to start at least 6 million PLHIV on TPT) were met early and by 2023, approximately 47% of the 39.9 million people estimated to be living with HIV had been started on TPT.⁴⁶ In 2024, 58% of people with HIV newly enrolled on ART were initiated on TPT and the global target of 90% coverage by 2027 remains significantly off.⁴⁷ Ongoing challenges to reaching this goal include local supply chain bottlenecks resulting in stockouts at facility level, refusal to initiate TPT by PLHIV, and lingering uncertainty from providers about excluding TB disease before prescribing TPT and development of drug resistance.⁴⁸
- Household contacts aged under five:** There has been a significant increase from 90,000 children initiated on TPT in 2015 to 1.77 million in 2024. One stakeholder opined there may be further increases following WHO prequalification of the paediatric friendly formulation in 2024 and depending on resource prioritisation. Expert opinion is that many countries continued using isoniazid monotherapy for children as paediatric rifapentine formulations became available later.
- Household contacts aged five and over:** This group has seen the largest increase in TPT provision from negligible number in 2015 to 2.8 million in 2024. Since 2021, it has expanded rapidly, rising from just over 10% of total TPT coverage to more than 50% in 2024. This increase is likely to reflect the uptake of 3HP in

⁴⁵ Based on data from 52 countries in 2021 and 86 countries in 2026 where rifamycin-based regimens were adopted. WHO (2025) Global Tuberculosis Report

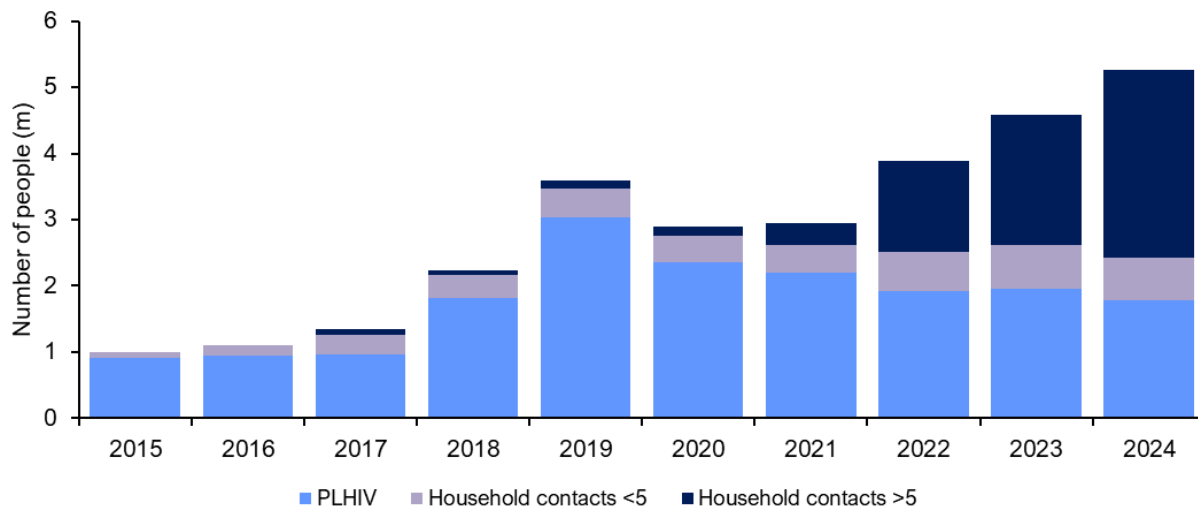
⁴⁶ WHO (2024) Global Tuberculosis Report

⁴⁷ Most national policies are for a single course of 3HP for people with HIV newly enrolled on ART. Only Zambia has indicated intention for multiple dose of 3HP for this population.

⁴⁸ See, for example, Timire C et al. Evaluation of Tuberculosis Preventive Treatment Uptake Among People Living with HIV in PEPFAR-Supported Facilities in Zimbabwe and Mande R. Preventive Treatment in People Living with HIV in Uganda: Facilitators and Barriers for Initiation and Completion. Trop Med Infect Dis 2025 Oct 18;10(10):296. doi: [10.3390/tropicalmed10100296](https://doi.org/10.3390/tropicalmed10100296)

India, which came after the close of I4TB country focused work (“I saw *Unitaid* was a catalyst... helping countries... especially in India... it really helped to sort of expand TPT to non-PLHIV, to household contacts.” – Global Stakeholder) (see Box 6).

Figure 2.8: Uptake of TPT (all regimens) among priority populations 2015-2024⁴⁹



Most of the above uptake has been for 3HP, given only 3HP is recommended by WHO for PLHIV taking DTG-based regimens. The 1HP regimen is also significantly more costly (US\$18 per 1HP adult course, compared to under \$US10 per 3HP adult course). Due to this 1HP may be more likely to be used where HIV prevalence is lower and there is a high TB burden, such as in India.



Box 6. Barriers to household contact TPT from India

Globally, the lack of routine contact investigation limits the uptake of 3HP among this population and there is a need for high burden countries to expand contact investigation further to reach higher coverage of the estimated population in need of TPT.

As discussed in multiple country level consultations including in India, the main delivery bottleneck now is not the drug itself but latent TB testing for HIV-negative adult contacts, which may limit efficient use. Although the reason for this is not fully clear, it is potentially due to the TB infection testing policy approach in India which differentiates by population, with PLHIV and children under five not requiring TB infection testing before TPT whilst HIV-negative contacts may be expected to have evidence of TB infection (confirmed through Tuberculin Skin Test (TST) or Interferon-Gamma Release Assay (IGRA)) before receiving preventive treatment).

There is limited access to IGRA, which requires drawing blood and more sophisticated laboratory services and TST has practical constraints such as availability of the commodity, limited accuracy in some populations, trained staff and need for a return visit to the provider for reading of the result, which can reduce completion of the care cascade. This context is evolving as new TB infection tests are now available that have advantages over TST and IGRA; however, these are not yet widely available.

Most of Unitaid’s conditions for global scale-up have been met, with I4TB having a medium to high contribution across all conditions.⁵⁰ Figure 2.9 shows the progress in achieving global conditions for scale-up

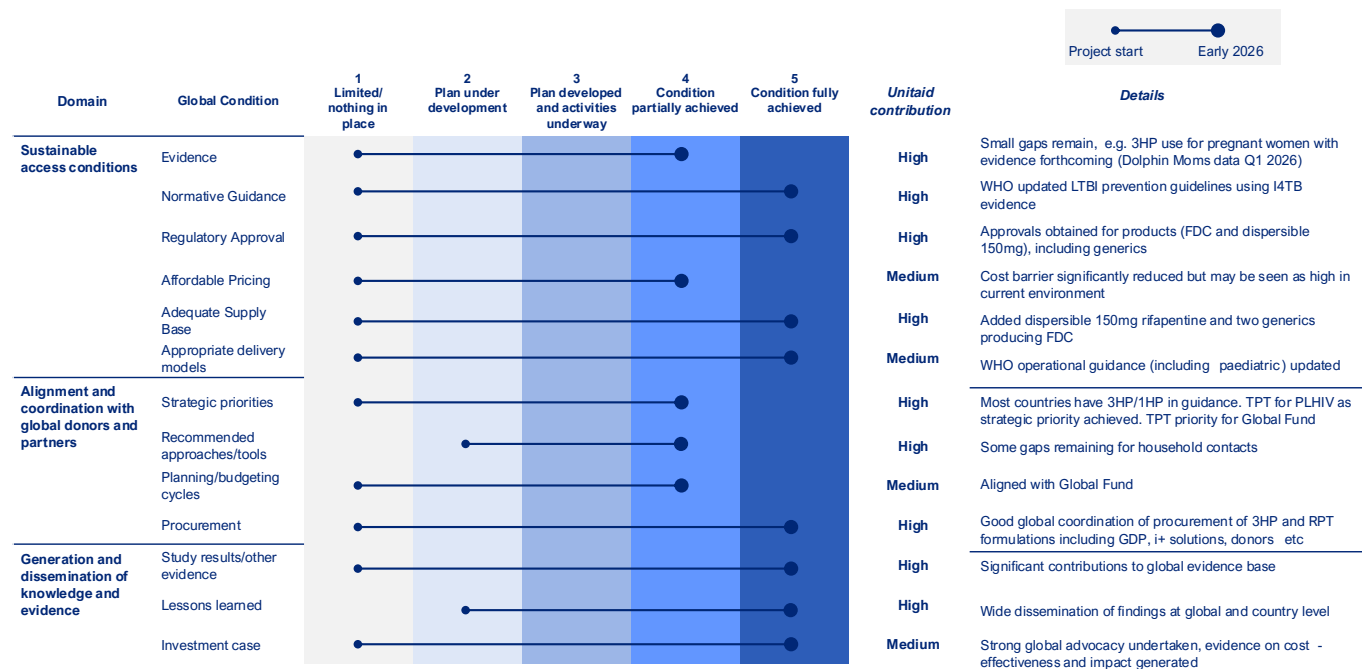
⁴⁹ WHO (2025) Global Tuberculosis Report

⁵⁰ At the start of I4TB in 2016, most Unitaid global scalability conditions with respect to 3HP for (i) sustainable access; (ii) alignment and coordination with global donors and partners; and (iii) generation and dissemination of evidence were limited/only under development. By project close, all conditions have been partially or fully achieved (Appendix H).

and Unitaids contribution. Progress was achieved through close collaboration with key global partners, including WHO, the Global Fund, and PEPFAR. Key areas of achievement include in sustainable access conditions (e.g. availability and affordability of FDCs and paediatric-friendly formulations), coordination with other donors – noting the exceptional circumstance in 2025 of the USAID stop work order and US funding overall, and high I4TB contribution to generation and dissemination of evidence.

Furthermore, as per the Target Access Profile (TAP), all access conditions were either largely or fully on-track in 2024. The one exception was financing.

Figure 2.9: Global conditions for scale up and Unitaids contribution⁵¹



Source: CEPA analysis of data provided by Aurum and Unitaids

I4TB helped countries establish most of the conditions required for sustained scale-up by the close of the initial project in 2022. All 12 original I4TB countries have since continued scaling and procuring 3HP and/or 1HP. By country project close out in 2022, countries had made significant progress toward scale-up as per the Unitaids country scale-up conditions. Project reporting in 2022 indicates 10 out of the 12 I4TB countries assessed most country scale-up conditions as ‘condition fully achieved’ or ‘condition particularly achieved and plan in place for how remaining gaps will be filled’. Exceptions to this assessment were Mozambique and Tanzania which had progressed less well due to delays in the adoption of 3HP as the standard TPT regimen for PLHIV in Tanzania and the decision in Mozambique to use up existing stock of isoniazid before introducing 3HP.

As country-level implementation under I4TB concluded, many countries had already integrated rifampine-based TPT into Global Fund, PEPFAR, or domestic financing mechanisms, supporting scale and sustainability beyond the project period. Since 2022, country reporting to WHO indicates the following progress in coverage (Figure 2.10 and refer to the Scalability Appendix in Appendix G for more detail):

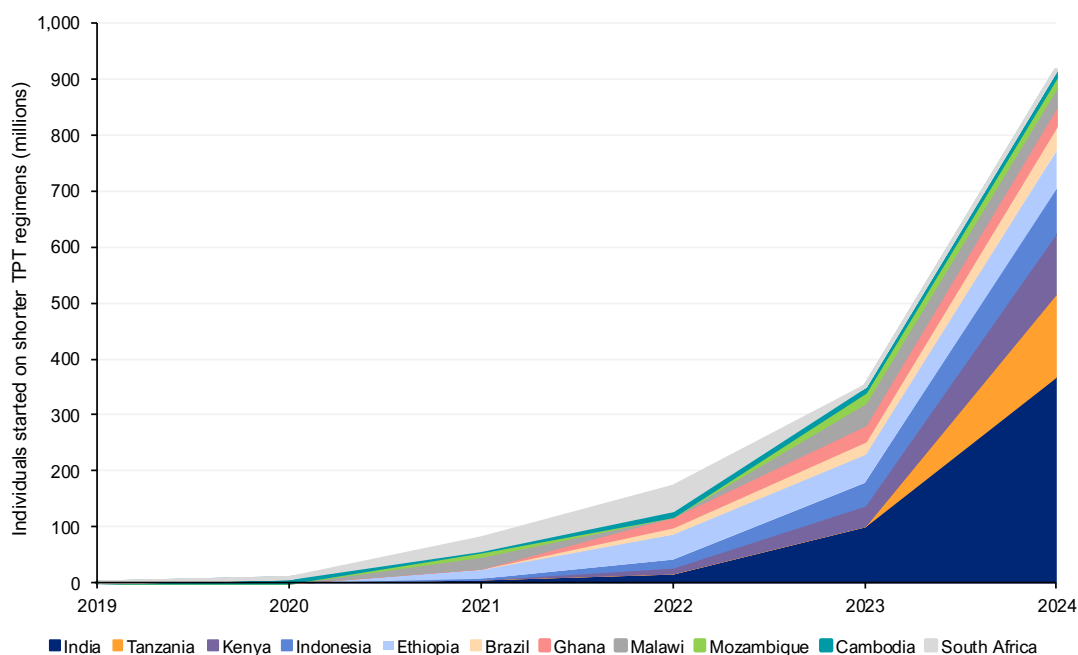
- For all countries with available data since 2022, there has been an increase in the number of individuals started on shorter TPT regimens containing rifampicin or rifampine.⁵² Countries with the largest absolute

⁵¹ Project start scoring and initial perception of progress achieved by early 2025 as per Unitaids Scalability Framework March 2023 as filled in by Aurum. Some adjustments to progress achieved and details is CEPA analysis.

⁵² <https://data.who.int/dashboards/tuberculosis>. No data since 2022 for South Africa and Zimbabwe

increases in initiations over 2020-2024 (ranked in order) were: **India, Kenya and Tanzania**. In India, uptake of 3HP was slower under I4TB due to India's own regulatory processes, but then had the largest scale up in more recently.⁵³ In Kenya progress likely built on the good gains made during I4TB implementation as described in Section 2.2.2. In Tanzania, this absolute increase is potentially due to a very slow start in uptake of TPT so the increase between 2023-2024 could reflect 'catch up' numbers. As India accounts for 25% of global TB cases, the sizable number of TPT initiations relative to other countries is not unexpected.⁵⁴

Figure 2.10: Initiations of shorter TPT regimens containing rifampicin or rifapentine in I4TB project countries 2019-2024 (WHO 2025)⁵⁵



- TPT coverage for PLHIV (longer and shorter regimens) continues to outperform other priority groups, though is variable by country (Appendix Figure F.2). Ghana and Mozambique have made notable progress in coverage for household contacts over time, performing better than other I4TB countries in 2023 and 2024 (Appendix Figure F.4). Whilst not stated in consultations on in project documentation, one of the reasons for Ghana's success could be because of Private-Public Mix (PPM) approach where free TB diagnostic and treatment services have been integrated into private healthcare facilities, including TPT.⁵⁶ In some districts in Mozambique, there have been additional efforts to reach TB contacts through community-level TB screening which may have aided coverage.⁵⁷

Despite the clear success of 3HP uptake in focus countries and globally during the project period, there are some remaining challenges. After the initial push to ensure all PLHIV already on treatment had a round of 3HP, demand dropped off and may remain uneven.⁵⁸ This reality, coupled with suboptimal contact tracing, has resulted in

⁵³ Progress remains significantly below global targets however.

⁵⁴ WHO (2025) Global Tuberculosis Report

⁵⁵ Zimbabwe did not report any data to WHO

⁵⁶ <https://www.afro.who.int/countries/ghana/news/united-against-tuberculosis-ghanas-private-and-public-health-sectors-join-forces>

⁵⁷ <https://www.stoptb.org/mozambique-fc-sds-project>

⁵⁸ Demand may depend on national policies regarding repeat or intermittent TPT for PLHIV. WHO guidelines do not specify, thus most countries are implementing one round of treatment but some countries (e.g. Zambia) are considering more than one round.

uncertainty for manufacturers and donors (“The need might be there, but the demand is not there...because programs aren’t doing contact tracing.”).

3. How well have the investment and Unitaid disseminated knowledge, evidence and lessons on equitable access? To what extent has this contributed to broader awareness/ support for these investment areas?)

Finding 8: The Unitaid TPT portfolio, particularly I4TB, effectively disseminated evidence at global and country levels, helping to build awareness and support for short-course TPT scale-up. It also promoted more equitable access by generating and sharing evidence for underserved populations, including children and pregnant women.

Strength of evidence	Rationale
 High	Strong consensus from global and country level consultations, supported by documentary and data evidence (e.g. journal articles, conference posters).

I4TB generated a substantial body of evidence that stakeholders reported was disseminated widely through academic publications, global conferences, technical and policy forums, coordination platforms, and country-level engagement activities. Dissemination channels included peer-reviewed journals (e.g. *Lancet HIV*), presentations at major conferences (e.g. Union World Conference on Lung Health, Conference on Retroviruses and Opportunistic Infections (CROI), technical working groups, policy meetings, webinars, handbooks, technical assistance materials, community engagement activities, and national dissemination events.⁵⁹ I4TB colleagues “spoke anywhere people would listen.”

Stakeholders noted the efforts made under the portfolio to focus on different population groups, including those who have previously received less attention, e.g. through the inclusion of pregnant women and children in studies. Overall stakeholders were complementary with the one area for improvement being males as some stakeholders consider them to be an underserved TB population group. The three strategies/programme sources show a move toward people-centred, community-based and digital innovations for TB screening, contact investigation and TPT, but they do not appear to explicitly prioritise males as a target group for TPT or screening innovations. Strengths in I4TB’s approach to knowledge sharing and influence include:

- **Provision of practical and implementation-oriented evidence.** I4TB was widely praised for sharing not only clinical and market evidence, but also practical implementation lessons related to adoption, demand generation, and scale-up. The consortium, including the I4TB website and BENEFIT Kids activities, was frequently described as a trusted “hub of knowledge” for global and country stakeholders.
- **Dissemination of findings through high-visibility platforms.** Findings were presented at major global conferences and large country dissemination events, supporting broad visibility and uptake of evidence across technical, policy, and donor communities.
- **Use of convening power to accelerate global uptake.** Stakeholders highlighted Unitaid’s important role as an influencer and coordinator, particularly through engagement with WHO, donors, and global technical partners.
- **Sharing of emerging evidence rapidly to support policy action.** Stakeholders reported that I4TB and BENEFIT Kids communicated new findings quickly to WHO, contributing to timely guideline updates and policy discussions.

⁵⁹ Aurum (2026), Increase Market and Public health outcomes through scaling up Affordable Access models of short Course preventive treatment for TB (IMPAACT4TB). Final Project Report

- **Generation of country implementation evidence to catalyse wider adoption.** Demonstration studies from countries such as Zimbabwe, Ethiopia, and Cambodia were viewed as influential in encouraging broader country uptake of rifapentine-based TPT. These early adopters provided data and lessons learned that supported discussions in other countries, for example, in Tanzania, where data from Ethiopia was presented to the TPT technical working group and lessons from their implementation experience were used to inform their planning for introduction and scale up of 3HP for PLHIV.
- **Investing in community-centred communication and engagement.** Community engagement activities were seen as highly effective in supporting scale-up, including translating complex technical issues, such as nitrosamine impurities, into accessible messages. Stakeholders also noted that early involvement of community members in project co-creation and research activities strengthened trust and support for TPT introduction.



Box 7: Country evidence dissemination

In **Cambodia**, the dissemination of knowledge and evidence from I4TB is considered to have been highly effective, utilising both formal institutional channels and innovative digital platforms. This included lessons being shared through monthly online supervision meetings and dedicated Telegram discussion groups for healthcare providers and patients. The WHO established a specific knowledge-sharing platform to distribute monthly updates on disease prevention to stakeholders

In **Indonesia**, dissemination is considered by stakeholders to have been effective at technical and policy levels (training, seminars, guidelines), but that more could have been done in relation to demand generation. That said, civil society-led dissemination was noted as being valuable including community workshops and cascaded dissemination which strengthened understanding of TPT, addressed misconceptions, and supported adherence, particularly among PLHIV.

In **Zimbabwe**, dissemination of project lessons and evidence was coordinated through the Zimbabwe MoHCC and project communication strategy by CHAI, disseminating information at district and provincial meetings, and national quarterly review meetings. In most cases, presentations were done at other convenient meetings, e.g. provincial nurses' meetings and national TB stakeholder meetings. The NTP and CHAI were noted to use every available and appropriate opportunity to make a presentation on 3HP. This multi-level communication strategy ensured that policymakers, district and facility staff were equally informed. To provide information on implementation, the project distributed dosing wheels for adults and children, alongside leaflets and patient guide booklets at relevant levels of the health system, along training activities.

In **India**, demand and uptake were helped by global I4TB materials and learning from other countries, especially South Africa, which were shared with Indian decision-makers.

2.3.2. Impact and sustainability

4. How impactful and sustainable is the progress achieved and what gaps remain, also in view of the financing context?

Finding 9: I4TB is estimated to have directly averted 1,950 TB cases in target sites across the 12 project countries by 2022. Its projected catalytic impact is 1,504,000 TB cases averted by 2030 through 3HP and 1HP, though this is highly sensitive to scale assumptions.

Strength of evidence	Rationale
 Medium	The finding is supported by only documentation evidence, and this is limited (e.g. modelling results, coverage assumptions).

John Hopkins University (JHU) estimated the impact of I4TB on TB cases using both direct and catalytic modelling approaches.⁶⁰ The direct estimate was based on procurement of short-course TPT in the 12 I4TB countries through the end of 2022, while the catalytic estimates considered additional procurement of 3HP and 1HP in both I4TB and non-I4TB countries through 2024. These estimates were compared against a counterfactual scenario assuming lower TPT coverage and continued reliance on isoniazid preventive therapy (IPT) alone. Their estimates indicate 1,950 TB cases averted directly through the project and 1.5 million by 2030 through catalytic impact.

However, the coverage assumptions used in the modelling are uncertain. The model assumed that by 2024, countries would achieve 80% TPT coverage among PLHIV newly initiated on ART and 20% coverage among PLHIV already on ART. In practice, recent WHO data cited above indicate that coverage among PLHIV newly enrolled on ART reached 58% in 2024, only a modest increase from 56% in 2023. This suggests progress toward the modelled target but at a slower pace than anticipated. For household contacts, the model assumed 50% coverage by 2030; by 2024, coverage had reached 25%, up from 20% in 2023, indicating somewhat faster recent progress in this population group. In a more constrained financing context, it is likely further scale and impact will be through less donor dependent countries with a high TB burden.

The box below provides evidence on improved impacts from 3HP use in project countries.



Box 8: Contribution of TPT to TB outcomes in I4TB countries

In **Cambodia**, through providing high-quality TPT to high-risk groups, such as household contacts of likely infectious patients and PLHIV, TPT is now recognised by national stakeholders as one of the significant factors in decreasing TB incidence across Cambodia (Cambodia's TB incidence fell from 308 per 100,000 in 2018 to 272 per 100,000 in 2024).⁶¹ The introduction of the 12-dose 3HP regimen has transformed treatment adherence. Completion rates are remarkably high, reaching 98% to 100% in several cohorts, with treatment abandonment described as "almost non-existent".

In **Zimbabwe**, there is a strong professional perception that the project contributed to the observed decline in TB incidence and mortality. The weekly dosing for three months is perceived to have improved adherence and completion rates, thereby enhancing the protective effect against TB disease. However, multiple stakeholders emphasized that there is currently no definitive data or completed impact studies to validate these perceived successes.

Finding 10. Sustainability risks are emerging around financing, civil society capacity, and long-term market security.

Strength of evidence	Rationale
 Medium	Finding supported by global and country level stakeholder consultations but the risks are still uncertain, especially in relation to financing given the changes to the global health financing landscape are only recent.

- Reduced global financing presents a growing risk to sustained TPT scale-up.** Stakeholders reported that TPT procurement volumes remained relatively stable between 2024 and 2025, although growth was expected to be higher prior to reductions in global health financing. Funding for TPT in 2025 continued to come from a mix of domestic budgets, the Global Fund, the World Bank, and bilateral donors. However, reductions in US Government funding which represented approximately half of international TB donor financing in 2024, including contributions through the Global Fund⁶², raise concerns that countries may

⁶⁰ John Hopkins University (2025), Final Estimates of IMPAACT4TB Impact and Cost-Effectiveness

⁶¹ WHO (2025) Global Tuberculosis Report

⁶² WHO (2025) Global Tuberculosis Report

increasingly prioritise treatment of active TB disease over prevention. Available country data remain limited and mixed: among five I4TB countries reporting 2025 funding gaps, three reported increases in the gap (Indonesia, Tanzania, Cambodia (very small gap)) and two reported decreases (Ghana, Kenya) (Appendix F.4.). With lower funding overall for TB, there are concerns countries will prioritise TB treatment over prevention (*“TPT is very low... countries are prioritising treatment of active disease.” – global stakeholder*).

- **Civil society and community engagement structures remain highly vulnerable to financing shocks.** Many local CSOs and CBOs supported under I4TB were significantly affected by the 2025 funding reductions, with some forced to halt activities entirely. Stakeholders noted that, despite their critical role in treatment literacy, trust building, and demand generation, many community-based organisations remain heavily donor dependent and lack sustainable financing mechanisms.
- **Household contact investigation remains a major vulnerability for future market growth and supply security.** Stakeholders highlighted that adult household contact tracing is operationally complex, resource intensive, and vulnerable to de prioritisation in constrained financing environments. Additional barriers included limited point-of-care diagnostics for active TB and variation in national diagnostic policies as barriers to TPT initiation of household contacts. Because household contacts represent a major source of future demand for rifapentine-based TPT, weak and inconsistent implementation of contact investigation will continue to constrain demand forecasting and long-term market stability.



Box 9: Financial sustainability in Cambodia

In **Cambodia**, the project served as a critical catalyst for the introduction and scale-up of 3HP and successfully transitioned into national systems. However the primary risk is the restricted national budget. The Cambodian government currently lacks the financial capacity to cover TPT costs independently and is unlikely to seek additional government funding. Therefore future funding is currently viewed as dependent on the Global Fund.

Finding 11. I4TB was significant to Unitaids as its first investment with a south-based lead implementer and the partnership is viewed as mutually beneficial, with Aurum since becoming a key Unitaids partner.

Strength of evidence	Rationale
 High	Finding supported by global stakeholder consultations with strong from relevant stakeholders, supported by documentation.

Although I4TB predated Unitaids’ 2023–2027 strategy and its strategic pillar to “Foster inclusive and demand-driven partnerships for innovation,” the grant represented an important evolution in Unitaids’ partnership model. This was a positive externality from the grant. Aurum became Unitaids’ first Global South-based lead grantee and managed a consortium that included major global partners such as CHAI. Aurum was seen as demonstrating strong technical and operational leadership while also bringing implementation credibility from a high TB/HIV burden setting.

Stakeholders viewed the consortium model as highly effective, and combined strengths in market shaping, clinical research, community engagement, implementation science, and country-level technical support, allowing I4TB to address multiple barriers to rifapentine access simultaneously. Several stakeholders noted that the breadth of expertise within the consortium reduced duplication and enabled partners to focus on areas of comparative advantage. Unitaids was also widely seen as adopting a collaborative partnership approach with Aurum and consortium members throughout implementation. They highlighted that the investment contributed to Aurum’s institutional growth and global positioning: while Aurum was primarily South Africa-focused at the start of I4TB, it is now working across 27 countries and continues to expand related TB prevention activities (Figure 2.11).

Figure 2.11: Aurum global footprint 2025



From a timeliness perspective, the main period of I4TB country implementation coincided with the COVID-19 pandemic, which caused major disruptions to TB programmes globally. In 2021, a no-cost extension was approved to mitigate delays resulting from manufacturer impurity issues, which compounded COVID-19-related disruptions, and to allow completion of key studies and initial rollout of 3HP in project countries. A second no-cost extension was approved in 2024 to address ongoing operational challenges affecting evidence generation, including slower-than-expected enrolment, ethical approval delays, and product-related issues. In both instances Unitaids flexibility to respond to these challenges was viewed positively by respondents (aligned with relevance and coherence findings).

5. To what extent have the investments and Unitaids progressed opportunities for regional manufacturing and greener API production?

Finding 12: Unitaids investment appears to be a strategically relevant contribution to regional API manufacturing and sustainable TB product supply. Evidence of results remains limited, as the work is still at an early stage.

Strength of evidence	Rationale
Low	Low evidence given the recent Unitaids investment and limited stakeholder awareness of the work with CPT Pharma.

The I4TB investment includes funding for CPT Pharma (a generic manufacturer based in South Africa) for technology transfer of the rifapentine API flow synthetic process. CPT Pharma is currently optimizing the synthetic process using lab-scale equipment and the process for the pilot has begun, with demonstration batches expected to be available by December 2026.⁶³ This activity was funded by Unitaids in mid-2025 after US funding through United States Pharmacopeia (USP) ended following the dismantling of USAID⁶⁴, indicating an important role for funders like Unitaids during the funding crisis. This investment with CPT Pharma is expected to make a

⁶³ CHAI (2026), Interim Report: Assessment of CPT Pharma's Rifapentine Api Manufactured Using a Flow Chemistry Synthetic Process Developed By Usp/Medicines for All.

⁶⁴ The USAID initiative collaborated with Virginia Commonwealth University (VCU) to develop a new process to synthesize rifapentine API using continuous manufacturing which was transferred to CPT Pharma. USP (2024). USAID Announces Technology Transfer of Novel Process to Produce Active Pharmaceutical Ingredient for Key TB Medicine, Lowering Its Cost and Increasing Availability. Available at: <https://www.usp.org/news/usa-id-announces-technology-transfer-of-novel-process-to-produce-active-pharmaceutical-ingredient-for-key-tb-medicine-lowering-its-cost-and-increasing-availability> (Accessed 11 June 2026)

meaningful contribution to advancing opportunities for regional manufacturing and greener API production, although progress remains at an early stage.

This work aligns with Unitaids' wider climate strategy, which aims to support climate-smart health products by reducing the environmental impact of product manufacturing and supply while improving resilience and equitable access. The investment is also expected to strengthen regional supply security by supporting API manufacturing capacity in a country with a high TB burden, and in close proximity to other high-burden countries in Africa. This is particularly relevant given the concentration of global rifamycin API supply and the vulnerability of TB medicine supply chains to international disruption, as evidenced during the COVID pandemic.

Given the recency of Unitaids' investment, further evidence will be needed to confirm performance, impurity profiles, regulatory progress, commercial viability etc. in the future.

Scalability, Sustainability, Impact: Key lessons and implications for Unitaids

Key strengths

Refer also to the Demand and Adoption analysis of key strengths pertaining to country readiness to scale. In addition:

- The project **comprehensively** addressed global and country level conditions for scale up (as per the Unitaids scalability framework) across the priority access barriers through its simultaneous efforts targeting changes in the market and at country level. As per the scalability framework and TAP, strong progress was made in virtually all areas.
- **Collaboration and coordination with scale partners**, PEPFAR and Global Fund in particular at country and global level, through the I4TB consortium's partner network and Unitaids was a key enabler for scale.
- **Comprehensive and quick sharing of information** through multiple channels, comprehensively covering a wide array of topics (implementation, pharmaceutical science, market aspects etc) and promptly (e.g. with WHO to inform policy changes).
- **Targeting of some previously neglected stakeholder groups** such as pregnant women and children.

Areas for improvement

Risks for scalability and sustainability include:

- **Future growth in TPT initiation** is in part dependent on strong integration of TPT with screening for active TB disease, including efforts to roll out new POC diagnostics so that eligible individuals can swiftly be enrolled on TPT post-triage. **Overall, the scale of 3HP benefited from a strong funding environment for TPT in many high burden countries** which is not transferable to the current financing context.
- **Effective approaches and tools to address 3HP hesitancy** among providers, PLHIV and other eligible populations should be well understood, as these may have implications for adoption of future prevention tools.
- **API impurities** remain a threat to secure country supply of 3HP.

2.4. RELEVANCE AND COHERENCE

Assessment of relevance and coherence is conducted jointly given the substantial overlap in the topics prioritised.

6. To what extent is the TB prevention portfolio doing the right things in terms of responding to the needs of affected communities, adapting to changes in country context, and integrating equity and inclusion considerations into its approach?
7. How well does the IMPAACT4TB investment fit in the context of other TB prevention interventions, and in what ways is it adding value?

Finding 13. I4TB was a highly relevant and strategically designed initiative to address the access barriers to rifapentine-based TPT regimens. The mix of market-shaping, clinical and operational research, demand generation and advocacy laid the groundwork for 3HP worldwide.

Strength of evidence	Rationale
 High	Strong consensus from global and country level consultations, supported by documentary and data evidence

Stakeholders consistently emphasised that the integrated package of market shaping, evidence generation, implementation support and advocacy was necessary to overcome barriers to rifapentine access in LMICs. Overall, I4TB strongly demonstrates Unitaids' role as a catalytic investor in expanding affordable access to 3HP globally.

In terms of timeliness, responsiveness, partner selection: WHO prequalification of the Sanofi 150mg rifapentine product in 2017 had facilitated international procurement but did not create a competitive market.⁶⁵ Unitaids and I4TB foremost recognized that 3HP introduction and scale up among PLHIV, a priority population for TPT, required safety evidence on use alongside DTG. This was particularly important for sending positive market signals and securing engagement from major funders such as the US Government, who were hesitant to support 3HP in the absence of supporting data on use among PLHIV. Unitaids funding to Aurum, who had existing study sites in South Africa, supported rapid initiation of the DOPLHIN studies.

Unitaid leveraged its 'catalytic' role in the market shaping ecosystem with appropriate flexibility in instruments: As described in the assessment of supply-side investments, the market shaping component was flexible, including use of an adjustable purchase order in place of a buy-down as initially planned, and incentives with MacLeods and Lupin including the EMAN for paediatric formulations. This allowed Unitaids to adjust to specific opportunities and bring cost savings. It is notable that rifapentine is technically difficult and costly to manufacture compared with many standard TB drugs, meaning fewer suppliers are willing or able to enter the market and supply diversification will take time. In this context, sustained long-term market signals remain critical. Following Unitaids' initial interventions, subsequent support from MedAccess through a multi-year agreement helped reinforce longer-term market stability.

I4TB, and Unitaids directly, also contributed to shaping global TPPs, with Unitaids playing a key role advocating for an adult 3HP FDC. This was important for orienting the market to FDCs which are generally preferred by countries and patients given they simplify the treatment regimen, reduce the pill burden, and enable more streamlined procurement. The project also provided input to the Paediatric Drug Optimization's (PADO) deliberations on paediatric formulations, and decision to pursue 150mg scored rifapentine tablet rather than an FDC.⁶⁶ (*"I think that really, having also the early data [and] early lessons learned from the studies that were implemented under IMPAACT4TB, was useful to inform the decision of PADO TB in terms of whether to go for a fixed dose."* - Implementing partner and PADO advisory group member).

In regard to meeting the needs of affected communities, I4TB's relevance is evidenced through the following:

- **Strong CCSE** which engaged neglected populations and helped address government, provider and community negative perceptions TPT, which were starting from a "deficit". This was critical for national and

⁶⁵ WHO (2017), First rifapentine product prequalified.

⁶⁶ Insights from the Study 35 on pediatric 3HP included (i) desire by health stakeholders to maintain flexibility by loose rifapentine to allow use with other regimens as needed; (ii) countries already had child friendly isoniazid on essential medicines list (as used for TB treatment) and embedded in country supply chains. Perspective that shifting to a child friendly FDC might incur more cost and supplier uncertainty.

community demand and adoption of 3HP and community and civil society partners played a key role in retaining confidence in countries with stock affected by nitrosamine impurity.

- **Appropriately focused on priority populations and diverse country contexts, thus strengthening its relevance in terms of generating evidence and lessons learned.** The project included countries designated as high burden for TB, TB/HIV and DR-TB by WHO. India and Indonesia, two of the three highest TB burden countries in the world, were included in the 12 I4TB focus countries. I4TB also worked in countries that are transitioning to lower burden status per WHO (e.g. Cambodia and Zimbabwe) where high TPT coverage is particularly relevant to ultimately move towards elimination status. Focus countries therefore generated lessons relevant to the diverse contexts where TPT was currently being scaled up.
- **I4TB sought to ensure that the TPT regimen and service delivery were acceptable to communities,** working with the health system and communities to find the most promising approaches to achieve high coverage *“They did not only try to match, to find the right dose, but they also really looked at what the community wanted for these formulations.”* (Global technical stakeholder)
- **Inclusion of pregnant women and young children in clinical and implementation research.** The I4TB costed extension brought an additional focus on children and pregnant women which is evidence of Unitaids’ pathfinding role in addressing the needs of often neglected populations. In addition to the ongoing DOLPHIN Moms and DOLPHIN Kids⁶⁷ studies, and the EMAV for paediatric rifapentine, I4TB also supported the RPT Crush study⁶⁸, recognizing that in the absence of a child-friendly formulation of rifapentine, NTPs and providers needed data on the bioavailability of rifapentine if crushed and given with liquid. Even with the availability of a dispersible formulation, providers can confidently use a crushed tablet in the event of a stockout or in countries where the child-friendly version is not yet procured.



Gender considerations within I4TB

- Global TPT strategies and WHO guidelines do not identify males or females as priority groups for TPT on the basis of sex alone. Prioritization is instead based on TB exposure and risk of progression to disease, particularly among household contacts, PLHIV, and other high-risk clinical groups. However, programmes are expected to monitor equity and may need locally tailored approaches if sex-disaggregated data show that either men or women are being missed.
- I4TB did not consistently collect and analyse TPT uptake and completion rates by gender across countries, so it is difficult to draw conclusions about how the project varied in reaching men and women. As an example, in keeping with the global guidelines, the national TB strategies in Cambodia, Indonesia and Zimbabwe show a move toward people-centred, community-based and digital innovations for TB screening, contact investigation and TPT, but they do not explicitly prioritise males or females as a target group for TPT or screening innovations. In Cambodia, males are identified as having higher TB notification and poorer treatment outcomes but the response is not framed as gender specific. However, it is known (via multiple prevalence surveys) that TB is more common among men and that men and women face unique barriers to care, including different experiences with the stigma associated with TB.
- At the investment level, the DOLPHIN Moms study financed through the I4TB costed extension is a strong example of Unitaids contributing to closing the evidence-gap for pregnant women requiring TPT.

There are some I4TB insights on gender from data available from sentinel sites. For example, sentinel sites in Indonesia reported that uptake of 3HP among PLHIV was predominantly among males (96.7%) with a median age of 31 years. On the other hand, 66.4% of PLHIV on TPT from sentinel sites in South Africa were women and in Ethiopia, 62.6% were women. In Cambodia, the

⁶⁷ DOLPHIN kids studies the safety of 3HP for children living with HIV on DTG-based regimens.

⁶⁸ RPT Crush studied breaking or crushing rifapentine formulations for children.

PLHIV cohort of sentinel sites was almost evenly split between men and women (as reported in I4TB country closeout reports).

As suggested as part of the Demand and Adoption analysis of areas for improvement (Section 2.2.2), future TB prevention investments could more systematically engage private sector and workplace-based platforms to improve access for men and other underserved groups at elevated TB risk (similar to the private sector component of HIVST investment). This is also carried through into the evaluation's recommendations.

Finding 14: The I4TB project coordinated well with global and country stakeholders and presented a coherent portfolio along with other Unitaid TB prevention investments.

Strength of evidence	Rationale
 High	Strong consensus from global and country level consultations, supported by documentary and data evidence. Moderate-Low evidence on areas where internal coherence with Unitaid investments was weaker.

Global collaboration and coordination with key scale funders supported I4TB's catalytic ambitions. As described earlier in the report (particularly supply-side findings 2.2.1) Unitaid and I4TB coordination with key funders, including leveraging an existing ART coordination platform for 3HP, was a key enabler for market confidence and addressing supply-side challenges. WHO Enabler support also strengthened coherence between evidence-generated and guideline updates.

I4TB supported integration of rifapentine-based TPT with existing service delivery systems in countries and avoided the pitfalls of piloting new regimens as a parallel service. The project was able to leverage the existing HIV care and treatment infrastructure and align distribution of 3HP to PLHIV with the multi-month dispensing model already in place in many countries, particularly in Africa. The project avoided setting up parallel data collection systems and worked with National TB and HIV programs to integrate the most relevant TPT indicators for monitoring uptake and completion of TPT. It built on community health structures, working with local providers who were trusted members of the community to provide education and distribute 3HP to eligible individuals and monitor treatment to minimize the number of visits to the health facility.

In terms of internal coherence, the I4TB investment complemented Unitaid's broader TB prevention portfolio through its inclusion of solutions for children and other vulnerable populations, particularly alongside the Benefit Kids project focused on DR-TB. Recognising that the concurrent V-QUIN⁶⁹ study included only adolescents and adults, Unitaid identified an important evidence gap and, through Benefit Kids, supported generation of critical data on the use of levofloxacin for children exposed to DR-TB through the TB CHAMP study. Stakeholders overall view Unitaid's flexibility as a key asset in project execution and supported global scale. This included I4TB responding to requests from other countries for procurement and forecasting support (e.g. Pakistan); reallocating resources to Malawi and Zambia where stock already landed in country had to be destroyed due to impurities in country and 3HP faced a reputational crisis moment. **Some areas of weaker coherence were raised by a few stakeholders, related to Unitaid's grant development model and coordination of projects with overlapping aims.**

⁶⁹ WHO TB knowledge sharing platform: A5.1 Summary of TB CHAMP and V-QUIN clinical trials. Available at: <https://tbksp.who.int/en/node/2745>. The V-QUIN study focused on adult and adolescent household contacts of people with MDR-TB and evaluated the effectiveness of levofloxacin preventive therapy

- A few stakeholders also reflected on Unitaids extended **grant development process may, in some cases, potentially diminish opportunities of strong country alignment and responsiveness to emerging opportunities**. While that this was in part mitigated by Unitaids above willingness to be flexible – with Unitaids being intentional in maintaining flexibility throughout implementation - in the more constrained funding context where every dollar needs to be maximised and capacities are stretched, Unitaids may need to consider how to adapt its grant development approach and grant making more broadly to be even more responsive and nimble, recognising grant changes also incur transactions costs (as well as the impact of delays). Further, some stakeholders also noted the need for agility between grant approval and implementation (*“From any grant being awarded and for the things to be actually rolled out on ground, it can be anything from 8 months to a year”*)
- As discussed in demand and adoption findings, WHO ERC approval of I4TB research studies incurred delays which impacted the timing of study results and their dissemination. There were also some examples of weaker internal coherence between I4TB and CaP-TB in countries.

Relevance and Coherence: Key lessons and implications for Unitaids

Key strengths

- **Continue adopting a comprehensive approach either through direct Unitaids investment and/or partnerships.** I4TBs relevance stemmed from addressing multiple barriers to rifampentine access simultaneously (*This is addressed further in the recommendations*).
- **Invest early in evidence generation that unlocks policy and donor support**, with appropriate partner selection and study design. Through identifying a lead grantee, Aurum, with existing research sites, the key DOLPHIN studies could proceed relatively quickly and influence PEPFAR and WHO policies.
- **Use Unitaids global influence to shape products that meet country and community needs.** Unitaids played an important role in shaping WHO TPP for 3HP, including advocacy for an adult FDC and child-friendly formulations.
- **Continue prioritising populations historically excluded from research.** Unitaids consistently filled strategic evidence gaps by ensuring pregnant women and children were included in research and access efforts for rifampentine-based TB prevention.
- **Design interventions that integrate with existing health systems and community structures.** Rather than establishing parallel delivery systems, Unitaids-supported projects worked through existing health services and trusted community-based organisations, strengthening local ownership and supporting longer-term sustainability.

Areas for improvement

- **Strengthen coordination across related Unitaids investments to maximise coherence and learning.** While I4TB complemented other Unitaids TB prevention investments, there were some missed opportunities for stronger alignment and cross-learning between some projects.
- **Expand future TB prevention strategies to better reach men and other underserved populations.** While the strong focus on pregnant women and children addressed important historical inequities, stakeholders identified missed opportunities to develop targeted approaches for men, who often experience a higher burden of TB disease. Future investments could incorporate more context-specific and culturally relevant strategies to improve TPT uptake among men. This would also enhance demand.
- **Grant development and approval processes should be more streamlined to improve responsiveness. These should also consider opportunities to accelerate WHO ERB or alternative external study review processes.** Stakeholders noted that lengthy grant development timelines may limit Unitaids ability to respond quickly to emerging evidence, evolving country priorities, and opportunities for rapid uptake of new TB prevention tools. Delays in WHO ERB also impacted the timeliness of I4TB results and Unitaids should consider how to address other barriers which impact project relevance.

2.5. EFFICIENCY

8. To what extent was the I4TB project efficiently delivered?

Finding 15: I4TB operated in an efficient manner to invest resources wisely in established structures, processes and partners, and embedded planning and implementation with the key global and national TB actors, which also enhanced their credibility as a partner willing to collaborate with existing systems.

Strength of evidence	Rationale
 Medium	Strong consensus from global and country level consultations, supported by documentary and data evidence. Overall, less evidence in some countries due to stakeholder availability.

I4TB worked within existing systems at all levels of implementation to introduce and scale up TPT services for priority populations. Examples included:

- At a consortium level, the project avoided setting up parallel processes and leveraged existing relationships among consortium partners to integrate their work within established global and national level working groups and other stakeholders. They participated as observers in WHO guideline development groups and the PADO-TB group and provided timely data to inform their deliberations, as well as disseminating results at high level international meetings such as the UNION conference and CROI.
- At national level, I4TB worked with National TB Program managers to support annual procurement structures and Global Fund activity planning, integrating their planning with these processes instead of having separate meetings. They participated in Global Fund, PEPFAR, USAID and other donor coordination structures at country level to ensure their work complemented other key stakeholders and was not duplicative or out of alignment with their support to Ministries of Health. Country approaches also included working within the routine recording and reporting systems at national and subnational level, integrating the key TPT uptake indicators with local health information systems (often DHIS2-based) to avoid a parallel reporting structure that would have required more effort to collect, analyse and report data to district, provincial and national TB and HIV programs.

Additionally, I4TB worked with existing civil society partners on the ground, leveraging their credibility as trusted partners to implement advocacy and communication activities to support demand creation for TPT. In Malawi, collaboration with COWLHA was efficient not only at community level, where their status as trusted leaders and messengers was leveraged to support treatment literacy campaigns, but also at national level, where their ongoing participation in the Malawi Civil Society Network provided the opportunity to influence guidelines for specific populations prioritised for TPT. I4TB often worked with CSOs that had an established track record of work with specific populations (ex, youth, pregnant women, LGBTQ+ individuals, health care workers) to expand their capacity to support TB prevention as part of their larger scope of work.

The choice of market shaping instruments also brought efficiencies to Unitaids, notably the APO with Sanofi, which was cost saving and carried a lower administrative burden for partners. Savings could then be applied to other market shaping interventions within the project.

Lastly, I4TB leveraged research investments among consortium partners to that implementation lessons were shared among partners. The project used existing research platforms to support I4TB-specific studies, for example, in the DOLPHIN studies, which took place in the Tembisa site managed by Aurum that has years of experience with clinical trials and pharmacokinetic studies. Unitaids also co-funded studies to expand sample size and population, for example, with the TBTC Study 35 agreement. The partnerships between consortium members and integration of

new research activities into existing platforms allowed for cost sharing across studies and expedited some studies e.g. DOLPHIN.

In these ways, I4TB operated in an efficient manner to invest resources wisely in established structures, processes and partners, as opposed to creating new ones. They avoided duplication of effort and irrelevant activities by embedding their planning and implementation activities with the key global and national TB actors, which enhanced their credibility as a partner willing to collaborate with existing systems. The project also retained core staff across the various research studies, which allowed them to be efficient and complete fieldwork in timely fashion.

3. CONCLUSIONS AND LESSONS LEARNT

The evaluation findings provide the following overarching conclusions and lessons on: (1) the strategic relevance, coherence and design of I4TB and contribution to Unitaid's TB prevention portfolio; (2) the contribution of the investment to accelerating access to 3HP and 1HP TPT and catalysing scale-up; (3) Unitaid's role as a pathfinder, investor and influencer; and (4) value for money.

(1) Strategic relevance, coherence and design

I4TB was a highly relevant and comprehensive investment that directly tackled the key barriers limiting access to rifapentine-based TPT in LMICs. Although WHO had recommended 3HP and 1HP, uptake remained stalled by high rifapentine prices, limited supplier competition, unresolved clinical and operational questions, and weak confidence among countries and donors regarding implementation at scale. I4TB correctly recognised that these barriers were interconnected and required a coordinated market-shaping response that combined supply-side interventions, evidence generation, country implementation support, advocacy, and community engagement. I4TB's comprehensiveness was a strength of the overall approach, noting the comparatively large investment value for Unitaid (including costed extension), and long implementation period of over 8 years. Consortium leadership by Aurum, a South Africa based organisation was also a strength and the first time Unitaid had funded such a model. I4TB partners were well networked with key scale partners and made the most of country and global level dissemination opportunities for 3HP.

Unitaid also demonstrated important added value through I4TB's focus on children and pregnant women, populations long overlooked in TPT evidence generation and product development. Investments in market shaping to encourage market entry of paediatric formulations at the same cost as adult formulations, and implementation evidence, helped lay the foundation for more equitable access to rifapentine-based TPT.

Unitaid's TB prevention portfolio demonstrated strong coherence across complementary investments and partnerships encompassing both DS-TB and DR-TB, priority population groups including PLHIV and children, and pregnant women, and longer-vision projects on long-acting treatments. During the I4TB project implementation, coordination with WHO, PEPFAR, the Global Fund, GDF and others proved especially critical in aligning policy, procurement, financing and implementation efforts, while also helping navigate severe early supply disruptions caused by over-estimation of production capacity, quality concerns, and COVID-19-related shocks. Taken together, Unitaid's direct engagement and the I4TB investment positioned the organisation as one of the central catalytic actors driving the global shift towards shorter-course TPT and prevention more broadly.

(2) Contribution to accelerating equitable access to rifapentine-based TPT and supporting scale-up

I4TB made a transformative contribution to expanding the availability, affordability and uptake of rifapentine-based TPT globally. It facilitated market entry of the 3HP and 1HP FDC alongside paediatric friendly formulations. The project helped drive rifapentine prices substantially below the originator price for improved affordability to support scale, supported market entry and quality assurance of generic manufacturers, and strengthened global confidence in the long-term supply viability of rifapentine-based regimens. These gains sequentially helped unlock broader donor financing and procurement by PEPFAR, the Global Fund and countries well beyond the original project settings.

The investment also generated critical clinical and operational evidence that helped remove major barriers to policy adoption and implementation. This informed WHO normative processes and supported national policy updates across multiple countries, helping move rifapentine-based TPT from limited pilot introduction towards broader implementation and national and donor-supported scale-up.

Civil society and community engagement (CCSE) emerged as one of the project's most distinctive contributions. As one stakeholder reflected, *"TB preventive treatment was starting, not from zero, but from a deficit, when it came to community acceptability."* Community partners played a critical role in rebuilding trust, strengthening treatment literacy, countering misinformation, and sustaining demand, including during the nitrosamine impurity concerns.

Embedding CCSE within a market-shaping investment demonstrated that successful product introduction depends not only on affordable medicines, but also on public confidence and community ownership. These lessons will remain highly relevant for future TB vaccines and other interventions that require populations and health systems to transition to new products.

At the same time, major sustainability risks remain. Declining global financing and the effects of the 2025 USAID stop-work order have created uncertainty for long-term market security, continued TPT scale-up, and support for CCSE. TPT coverage remains far below the 2027 global 90% target, and sustaining the rifapentine market will require continued investment in contact tracing and household contact management to encourage demand, alongside development of future rifapentine indications beyond TPT (such as HPMZ).

(3) Unitaids role as a pathfinder, investor and influencer

I4TB and the broader TB prevention portfolio provide a strong example of Unitaids operating simultaneously as a pathfinder, investor and influencer. Figure 3.1 provides an overview of key project achievements and the specific Unitaids contribution.

It is reasonable to assume that without Unitaids investment, country introduction of 3HP would have been delayed by many years and reach smaller scale, given the questions on interaction with dolutegravir, high price and market risks at the time. Country demand would also have been slower in the absence of an FDC, potentially limiting supplier diversification. All this would have impacts on health outcomes, including for children who have benefitted from the dispersible rifapentine product catalysed through the EMAV.

Figure 3.1: Unitaids contribution assessment

Role	I4TB key achievement	Assessment of Unitaids contribution			Strength of evidence
		Low	Medium	High	
 Pathfinder	- Foundational DOLPHIN studies demonstrating safety of 3HP for PLHIV on dolutegravir, supporting market confidence in 3HP demand - Closed evidence gaps for groups often neglected in clinical and operational research (children and pregnant women). - Stimulation of generic 3HP and 1HP, including FDC	[Full bar]			High
		[Full bar]			High
		[Full bar]			High
 Investor	- Absorbed early market shaping risks for Sanofi and generic rifapentine formulations - EMAV for paediatric-friendly rifapentine, securing same price as adult formulation, and cheaper vs. alternatives - Global public goods: clinical and operational evidence in different epidemic and health systems contexts - Scale of 3HP for PLHIV and child and household contacts	[Full bar]			High
		[Full bar]			High
		[Full bar]			High
		[Full bar]			High
 Influencer	- Key brokering role with PEPFAR and partners to agree to US\$15 for Sanofi rifapentine product - Global TPP for adult 3HP FDC - PADO engagement to agree on a paediatric dispersible 150mg rifapentine in place of an FDC - Coordination with WHO, PEPFAR, the Global Fund, manufacturers, civil society and country stakeholders, helping shape discussions around TPT access, evidence priorities, pricing and implementation approaches.	[Full bar]			Medium
		[Full bar]			Medium
		[Full bar]			Medium
		[Full bar]			High

Key points are the following:

Pathfinder – Contribution: High

Unitaid demonstrated strong pathfinding leadership by investing in the foundational DOLPHIN studies which helped to enable PEPFAR entry into the 3HP market, and was recognised by TB actors as driving the TPT agenda for pregnant women and children. Commitment to generic market entry to foster a sustainable market for rifapentine

which had previously supported only the originator helped break through critical barriers related to pricing and supplier diversification.

Investor – Contribution: High

Unitaid played a strong catalytic investor role by absorbing early market and implementation risks that other funders were not yet positioned to support through the APO with Sanofi, and demonstrated nimbleness and flexibility to advance the agenda, using different market shaping instruments for different products, and different moments. I4TB generated important global public goods, including clinical and operational evidence, implementation learning, procurement coordination mechanisms, and early country implementation experience. Critically, it helped create the conditions for subsequent large-scale financing and procurement by PEPFAR and the Global Fund.

Influencer – Contribution: High

The investment also strengthened Unitaid's role as an influencer within the TB prevention ecosystem. Through coordination with WHO, PEPFAR, the Global Fund, manufacturers, civil society and country stakeholders, Unitaid helped shape discussions around early Sanofi price point, and the TPP for 3HP to encourage FDCs which are preferred by users and health systems alike. Stakeholders consistently recognised Unitaid as an important convening and enabling actor within the evolution of the global rifapentine market and broader TPT agenda.

(4) Value for money

Overall, the TB prevention portfolio, and I4TB in particular, delivered strong value for money against Unitaid's catalytic objectives, generating important gains across affordability, availability, evidence generation, policy adoption, and early market expansion for rifapentine-based TPT.

The investment's strongest returns came from accelerating global market readiness and momentum for rifapentine-based TPT — particularly through evidence generation, pricing and supply interventions, and enabling broader donor-supported scale-up. While routine large-scale integrated delivery remains incomplete in several countries, I4TB fundamentally reshaped the trajectory of rifapentine-based TPT and helped move the field from limited pilot introduction towards sustained global scale-up.

4. RECOMMENDATIONS

Recommendations are provided on: (i) Unitaid investments in TPT; and (ii) broader recommendations for Unitaid's grant-making approach across its portfolio, in support of its roles as a pathfinder, investor and influencer within the global health architecture. They integrate feedback from Unitaid, the I4TB consortium, and other key stakeholders consulted as part of the evaluation.

Part 1. Recommendations for Unitaid's investments in TPT

These recommendations consider three main trends relevant to TB responses:

- The significant shift in the TB funding and implementation context, most notably the dismantling of USAID, the largest bilateral donor for TB, as well as PEPFAR, along with overall tightening of health financing flows through the Global Fund and other partners.
- Emerging technologies that bring TB diagnosis closer to communities, including near-POC and tongue swabs which are prioritised in Global Fund Grant Cycle 8 guidance.⁷⁰
- Unitaid's strong credibility within the TB community, through I4TB and other investments as well as direct Unitaid engagement, as well as leadership in promoting equity and not leaving priority populations behind.

Recommendation 1: Consolidate remaining I4TB gains by (i) accelerating policy uptake relevant to priority populations, and (ii) supporting regional API manufacturing

The first two sub-recommendations could involve efforts undertaken through Unitaid's WHO enabler grant. They concern the DOLPHIN-Moms and DOLPHIN-Kids clinical studies on safety of 3HP with DTG. Study results were made available to WHO in March 2026 to inform guideline review, and will be released more widely at the 2026 International AIDS Society (IAS) and UNION conferences.

- Unitaid should collaborate with WHO to rapidly translate the forthcoming DOLPHIN-Moms and DOLPHIN-Kids evidence into updated global guidance and support timely country dissemination, in collaboration with TAG and other partners.
- Unitaid should collaborate with the Global Fund, WHO and civil society to support countries to incorporate forthcoming WHO guidance into Global Fund Grant Cycle 8 planning and national policies, using existing TB investments and partnerships to provide technical assistance, where needed. This approach is already being applied through Unitaid's Advanced HIV Disease grant to Aurum and other Aurum-led TB activities.
- Unitaid should assess the results of investment with CPT Pharma and identify opportunities for continued support if early results are promising. This could be linked with Unitaid's other regional manufacturing efforts.

Recommendation 2: Integrate TPT with new TB screening, diagnostics and community-based delivery to close the gap in TPT uptake - supporting more integrated, people-centred approaches for priority populations

- Unitaid should promote integration of TPT into community-based TB screening and diagnostic pathways, using portable digital X-ray/CAD in the near term, and emerging near-POC diagnostics and simplified specimen collection approaches as they become available.
- Unitaid should support implementation models that strengthen contact investigation and active case finding, recognising these are now among the principal constraints to expanding TPT.

⁷⁰ Global Fund (2026). Grant Cycle 8 (GC8) Prioritization Guidance: Tuberculosis. Available at : https://resources.theglobalfund.org/media/1b3b0pem/cr_gc8-tb-prioritization_guidance_en.pdf (Accessed 11 June 2026)

- Unitaid should continue prioritising integrated, people-centred approaches that bring TB services closer to vulnerable populations.

Recommendation 3: Sustain Unitaid's leadership in developing TB prevention and treatment options for underserved populations, including children and pregnant women

- Unitaid should explore strategies to accelerate country availability of child-friendly formulations. This could include engaging civil society for national advocacy and country support to address bottlenecks in product registration.
- Unitaid should build on I4TB lessons from paediatric market shaping. Where achieving price parity with adult formulations is not feasible, explore mechanisms to incentivize inclusion of child-friendly products in domestic financing strategies, and in Global Fund and other financing mechanisms.

Recommendation 4: Leverage Unitaid's influencer role to ensure TPT and complementary activities are covered as high burden countries plan for the transition to domestic financing

- Unitaid should bring the lessons learned from I4TB and other TB prevention projects, and its credibility in demand forecasting to inform national and subnational planning and budgeting processes. In some cases, it may be strategic for Unitaid and/or its partners to participate directly in domestic financing discussions.

Recommendation 5: Continue to position Unitaid for the next generation of TB prevention innovations

- Build on Unitaid's leadership in TB prevention by convening partners around future TPT innovations and preparing for TB vaccine introduction. Use Unitaid's convening role to help clarify delivery models, financing approaches and country readiness for future TB prevention technologies. The most promising TB vaccine candidate will likely not be provided through the traditional immunization programs and related strategies, and the role of National TB Programs and the wider donor community is unclear. Unitaid could be well placed to play a role in global planning for TB vaccine introduction at all levels.

Part II. General recommendations for Unitaid across investment areas

The following cross-cutting recommendations draw from the market shaping and CCSE learning themes and other insights from the evaluation and reflect the current health financing context.

Recommendation 6. Continue investing in integrated access strategies where relevant

- I4TB's effectiveness stemmed from addressing multiple barriers to rifapentine access simultaneously, including supply constraints, limited clinical evidence, lack of child-friendly formulations, weak demand, and policy hesitancy. Future Unitaid investments should consider this comprehensive approach, acknowledging I4TB's comparatively large value within Unitaid's portfolio.
- Future investments should strengthen alignment between supply and country demand activities, informed by robust review of production capacity and risks. This is particularly critical where there is a single supplier. The EMAN is a good example of aligning country readiness (e.g. policy) with supply.

Recommendation 7: Evolve Unitaid grant-making to improve speed and agility, whilst retaining Unitaid's flexibility within project delivery

- Unitaid should test more co-creation and flexible approaches to project development with implementing partners. This could include (i) targeted expressions of interest based on partner landscape analysis and early engagement; (ii) small number of strategic portfolio partnerships that provide a flexible 'call-down' mechanism, improving agility and reinforcing Unitaid's catalytic role. To inform options, Unitaid could scope the grant-making approaches of other organisations having a similar catalytic role. This could also inform early analysis for Unitaid's future strategy.
- Unitaid should continue enabling projects to adapt as evidence and implementation experience evolve, which was considered a strong value-add within I4TB.

- Unitaid should continue to encourage consortia with leadership based in the global South and maintain a strategy-level KPI to monitor progress. The Aurum Institute leveraged Unitaid's investment to strengthen its position not only in Africa but in other regions. In the current funding climate, Unitaid should build on this experience and identify additional promising partners who can lead multi-country projects throughout their portfolio. This could be part of a more intentional grant-making process (as in recommendation 6).

Recommendation 8: Address bottlenecks to shorten the pathway from evidence generation to policy impact

- Unitaid should review the value for money of its evidence generation approach to identify the mix of research approaches that delivers the greatest policy influence and country uptake.
- Unitaid should explore where appropriate, a greater emphasis on evidence generation approaches such as operational and implementation research that can more rapidly inform country policy and programme decisions. Such research should leverage and strengthen national data systems, using routine and real-time data to support adaptive implementation and accelerate learning.
- Unitaid should also work with the WHO Ethics Review Committee (ERC) to identify and address the main constraints within review processes without compromising scientific rigour.

Recommendation 9: Strengthen integrated, people-centred investment portfolios and the use of gender-based approaches

- New investments should consider opportunities beyond disease 'silos', drawing on resources such as Unitaid's recent landscape analysis of care pathways for populations at higher risk of tuberculosis. Unitaid is also supporting this through forthcoming integrated diagnostics investments.
- Strengthen gender and equity analysis during investment design and implementation, including routine use of sex-disaggregated data to identify gaps across the service cascade. Although I4TB wisely avoided the creation of parallel data systems to collect and analyze project specific data for routine reporting, it may be helpful to collect sex-disaggregated indicators at a subset of focus sites for a limited period of time to identify gender differences in the provision and uptake of interventions.

Recommendation 10: Continue to embed CCSE in Unitaid's work, with implementation timelines and financing that reflect the contribution to project outcomes

- CCSE contribution to project outcomes should be strengthened within results frameworks. Future investments should also explore more sustainable funding models than one-off grant cycles, strengthening organisational capacity where needed, and promoting longer-term financing mechanisms such as social contracting where appropriate.

APPENDIX A DETAILED EVALUATION METHODOLOGY

A.1. EVALUATION FRAMEWORK AND APPROACH

The evaluation framework (Figure A.1) is grouped in three pillars to include: (i) effectiveness; (ii) scalability, impact and sustainability, and (iii) relevance, coherence and efficiency. Within each pillar we have structured evaluation questions in a strategic and implementable manner (i.e., a manageable set of questions at a suitable level of aggregation). Key points are as follows:

- We have emphasised the **OECD DAC evaluation criteria** of effectiveness and scalability which aligns with Unitaids's strategic objective 1.
- There is a learning emphasis for this evaluation which is clearly highlighted in the framework through the **key learning themes** of (1) civil society engagement and (2) market shaping (which will cut across the evaluation questions).
- This is a **theory-based evaluation, using mixed-methods, and draws on the Theory of Change (ToC)** (Figure A.2). **Through contribution analysis** we review of the extent to which the impact pathways identified in the project ToC have played out in practice. Evaluation methods comprised document and data review, stakeholder interviews, deep-dive in-person country case studies, light touch remote country reviews and case studies on the learning themes. AI was used to support qualitative analysis supported with close human validation (e.g. through checking details, refining prompts or redoing analysis as necessary to reduce risk of hallucinations etc).
- The evaluation applies a **gender lens** with analysis of the extent I4TB considered gender in its overall approach and analysis, and provides insights for Unitaids what could be done in future investments to strengthen its approach to gender analysis and gender responsive programming.
- Finally, the evaluation applies a strong emphasis on a **utilisation focused evaluation** (e.g. ensuring the development of actionable recommendations that are viewed as appropriate and feasible), **an inclusive and community engaged approach** (to ensure all key stakeholders can contribute their views to this evaluation) and **robustness and scale-based conclusions** (e.g. use of a robustness assessment framework to assess quality and quantity of evidence supporting findings, employing a range of scale-based assessment frameworks including the strength of effect and level of contribution). Refer to Appendix A.2.

Figure A.1: Evaluation framework

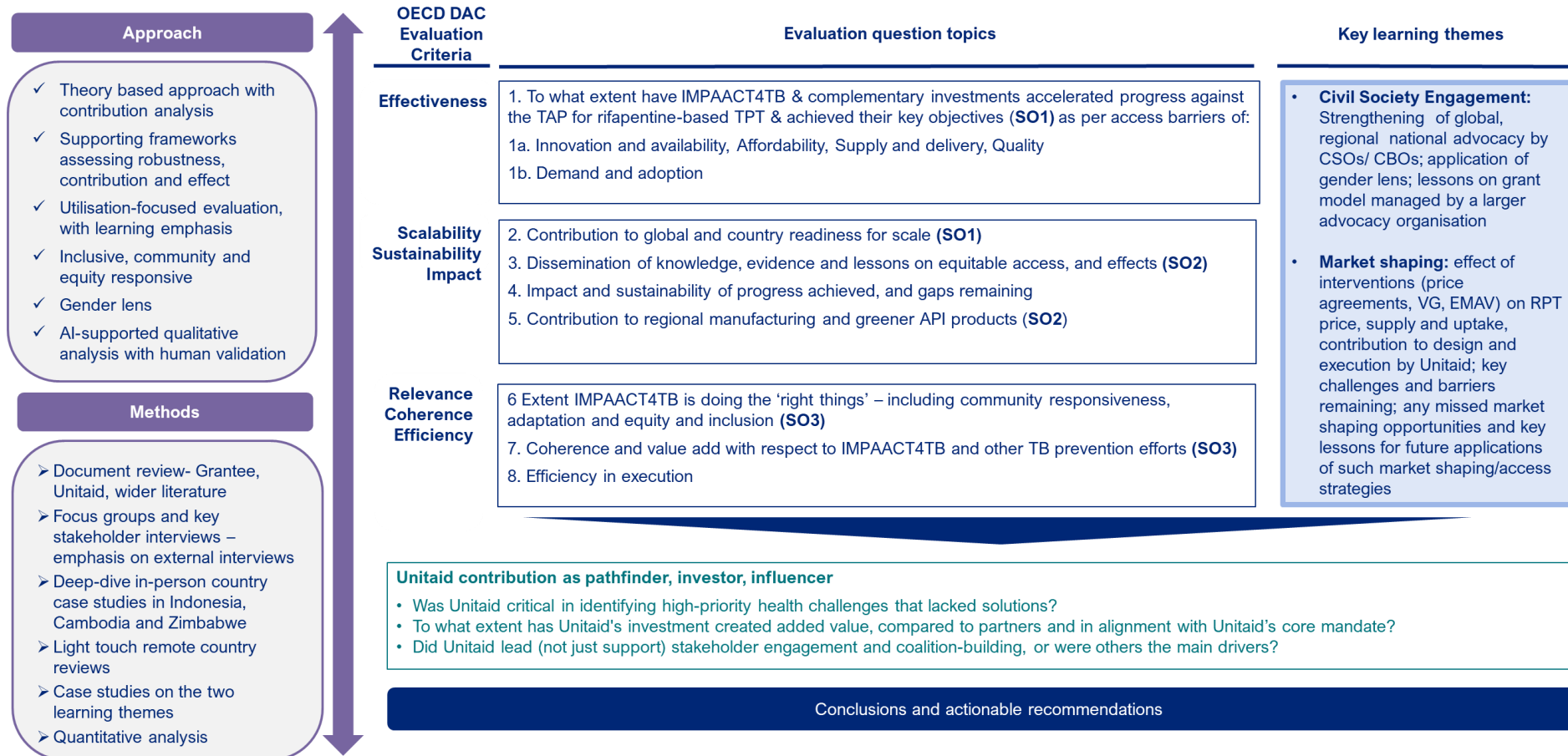


Figure A.2 presents the ToC for the ‘Enabling preventative treatment in high-risk groups’ portfolio as developed by Unitaid. The key investment in the portfolio is the Aurum IMPAACT4TB project with supportive investments including Stellenbosch BENEFIT Kids (closed); EGPAF CaP TB (closed), University of Liverpool, LONGEVITY (ongoing); WHO Enabler (ongoing), WHO PQ (ongoing) and MPP (ongoing).

Figure A.2: Unitaid Theory of Change for preventative treatment in high-risk groups

Public Health Need	Globally, one in four people are estimated to be infected with TB bacteria (latent TB) and of those, 5-10% progress to develop symptoms of TB. Household contacts, especially child contacts, and people living with HIV (PLHIV) are at greatest risk of progressing from infection to disease and experience worse health outcomes. The WHO recommends TB preventative therapy (TPT), yet uptake and completion levels remain low, especially for high-risk groups. Increased access to shorter, safer and more affordable TPT regimens and child friendly formulations will contribute to reaching global prevention coverage targets.			
Access Barriers	• Innovation & Availability: lack of child-friendly and long-acting formulations; evidence gaps on safety and effectiveness for use in key populations (esp. CLHIV, pregnant women) • Quality: lack of quality-assured rifapentine (RPT) based formulations; issues with API impurities • Affordability: high cost of 3HP; resource intensive service delivery needs for contact tracing • Supply & delivery: low volumes, lack of competition (single supplier) • Demand & adoption: Lack of WHO guidelines on RPT-based therapies for household contacts under two years of age and HIV+ pregnant women, as well as low uptake of RPT-based therapies in high-burden countries; limited evidence on feasible and cost-effective implementation strategies and operational barriers at the country level; gaps in awareness and advocacy			
Pathway to impact	Outputs	Expected Results (Outcomes)		Impact
	• Evidence generated for dosing, safety, and efficacy of 3HP/1HP for HHCs and vulnerable groups (CLHIV, pregnant women) and acceptability, feasibility, and cost-effectiveness of 1HP vs 3HP and for levofloxacin for MDR-TB prevention. Long-acting formulations • Generic suppliers supported to develop quality-assured RPT-based formulations and file with national regulatory authorities (NRAs) • Lower RPT price negotiated with suppliers of new formulations • Cost-effective and scalable models demonstrated for TB prevention delivery • Civil society organizations (CSOs) supported to lead demand creation and advocacy activities	Primary outcome (SO1): Accelerated introduction and scale-up of improved TPT to drive equitable access for high-risk populations in LMICs, supported through a sustainable market for affordable and quality-assured supply. 1. Catalyzed introduction of shorter RPT-based regimens in children through development of new pediatric formulations, expanding dosing for all ages, operational studies and roll-out support to countries through choice transition support, early market access and technical assistance. 2. Reduced cost and secured supply of quality-assured RPT-based formulations through market interventions. 3. Cost-effectiveness established and investment case developed to support advocacy for adequate programmatic funding for scale-up. 4. Strengthened normative and operational guidance for TPT in high-risk populations (children<2, CLHIV, PLHIV, pregnant women; MDR-TB child contacts, etc) 5. Expanded coverage of RPT-based TPT regimens for high-risk populations in project countries and beyond Supporting outcome (SO2): Create systemic conditions for sustainable equitable access 1. Implementation resources and key lessons/takeaways developed and widely disseminated 2. Pathway identified for cheaper, greener, and diversified API supply and manufacturing for rifapentine.	Supporting outcome (SO3): Foster inclusive and demand-driven partnerships for innovation 1. Strengthened national TPT platforms, bringing together MOH departments, community groups, people with lived experience and others to ensure inclusive technical and operational decision-making and coordination and greater accountability. 2. Enhanced capacity and financing of CSOs and networks to design, lead and scale up country/regional advocacy, demand generation and community-led monitoring. 3. Donors and governments engaged and aligned on roll-out of comprehensive and integrated TPT approaches in LMICs	Public Health Impact • Reduction in TB incidence and deaths among PLHIV and HHCs • TB cases averted • Lives saved among PLHIV and HHC Economic Impact • Health system efficiencies to scale interventions and introduce new tools Equity impact • Family friendly formulations available to reach additional at-risk populations
Key Risks	• Strategic: Prices remain higher for RPT-based formulations, especially for 1HP, undetermined nitrosamine clearance threshold for pediatric products • Implementation: research delays; time and costs to resolve nitrosamine contamination issues; market may favour 3HP over 1HP due to higher daily pill burden, cost, and other factors • Sustainability/Scalability: The scale-up environment is more difficult for prevention interventions and costs for contract tracing remain high; there are opportunities to leverage support from partners and to mobilize domestic resources.			

A.2. STRENGTH OF EVIDENCE FRAMEWORK

We assess the strength of the evidence by assessing both the:

- *quality of the evidence*: this includes the consistency and potential for bias. For example, relating to the documentation and feedback this would include considering aspects such as the source and reliability of the quantitative data and qualitative information (where possible/relevant), and involvement of the consultee providing feedback on a specific issue (e.g. implementers may be conflicted to provide positive rather than critical feedback, etc.).
- *quantity of the evidence*: this includes the amount and diversity of evidence. For example, we assess the extent to which findings are consistent after being triangulated across sources of information. In terms of consultations, we consider how many consultees responses will support the same view, or instances in which views might have been contradictory.

Bringing together these aspects, Table A.1 presents our strength of evidence framework. All robustness rankings are *relative* robustness rankings, based on careful consideration and are ultimately judgement-based.

Table A.1: Robustness rating for emerging themes/main findings

Rating	Assessment of the findings by strength of evidence
High (4) 	• The finding is supported by multiple sources of data of generally good quality, allowing for robust triangulation including documents, different stakeholders in different contexts and majority of consultations (both quantitative and qualitative sources)
Medium (3) 	• The finding is supported by a few data sources of good quality, limited triangulation, where corroborative sources allow for reasonable but evidence coverage not complete.
Low (2) 	• The finding is supported by very limited evidence (1 or 2 sources) or by multiple sources of lower quality and no triangulation
Insufficient (1) 	The finding is supported by incomplete or unreliable evidence or contradictory consultations. Should not be included in report

APPENDIX B BIBLIOGRAPHY

This annex provides the list of documents and references used for this report.

B.1. IMPAACT4TB

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APPENDIX C CONSULTTEE LIST

Table C.1 presents a list of stakeholders interviewed.

Table C.1: Stakeholders interviewed

Organisation	Name	Role
Unitaid		
Unitaid Secretariat	Tanya Guenther	Monitoring and Evaluation Manager
	Mariam Toure	Technical Officer
	Evaezi Otuorimuo	Programme Officer
	Cherise Scott	Senior Technical Manager, Strategy
	Dessislava Tarlton	Technical Manager, Access
Former Unitaid / Current independent	Ademola Osigbesan	Previously market shaping focal point for I4TB at Unitaid
Aurum		
Aurum Institute	Gavin Churchyard	Principal Investigator / senior project lead
	Violet Chihota	Chief Scientific Officer
	Jeff Weiser	M&E lead
	Neesha Naridus	Finance manager
	Daphne Van der Wind	Grant manager / reporting and grant management
	Makaita / Maka Gombe	IMPAACT4TB project lead / market access director
	Hudaa Croeser	Communities and communications / tools development
Grantees (global level)		
KNCV Tuberculosis Foundation	Agnes Gebhard	Director Technical Division
Treatment Action Group	Mike Frick	Co-Director, TB Program
Johns Hopkins University	Nicole Salazar-Austin	Faculty / paediatric trial lead
EGPAF / CaP-TB	Martina Casenghi	Director, TB Program
CHAI	Aman Siwach	Senior Director, Global Markets team
	Shamim Mannan	IMPAACT4TB project implementer
	Blen Kebede	Senior Programme Manager, Global TB Team
(previously) iPlus solutions	Wesley Kreft	Procurement / supply role
Stellenbosch University / Desmond Tutu TB Centre	Anneke Hesseling	Director
Technical partners (global)		
WHO	Kerri Viney	Team Lead
	Annemieke Brands	Technical Officer
WHO Prequalification	Wondiyfraw Wordu	Pharmaceutical assessor

Organisation	Name	Role
WHO	Dennis Falzon	Team Lead on TB prevention and treatment
	Avinash Kanchar	TB preventive treatment technical officer
GDF	Brian Kaiser	Technical Officer
PADO-TB	Tiziana Masini	Consultant
PAHO	Christopher Lim	Unit Chief
MSF	Cathy Hewison	Technical Partner
	Ana Paula Oliveira	Technical Advisers
Global Fund	Eliud Wandwalo	Head of TB portfolio
	Celeste Edwards Gracia	Senior TB/HIV Disease Advisor
USAID	Cheri Vincent	Division Chief, USAID TB Team
US CDC	MacArthur Charles	Physician
MedAccess	Asif Ali	Health Markets Access Director
	Evans Mburu	Head of Implementation
Manufacturers (global)		
CPT Pharma	Hannes Malanes	Co-owner
MacLeod's	Sailesh Pednekar	President – International Business
Cambodia country assessment		
CENAT	Huot Chan Yuda	Director
	Onn Siphann	Deputy Director
	Nou Chanly	Chief of Technical Bureau
NCHADS	Narom Prak	Deputy Director
US State Department	Song Ngak	Technical Advisor
WHO	Deng Sarongkea	Advisor
CHAI	Seak Kunrath	Program Manager for Assistive Technology and Tuberculosis
	Chay Sokun	Medical Advisor
KHANA	Choub Sok Chamreun	Director
CHC	Heng Bunsith	Executive Director
	Nak Savoeun	TB Program Manager
	Sen Phaloday	M&E Coordinator
NIPH	Pall Chamroen	Lecturer and former KHANA researcher
Kampong Chhnang Province Public Health District	Thab Sothea	TB Advisor
Kampong Chhnang Province Preaskosomak Health Center	Ean Rortha	Director and MD
	Pann Bunthorn	Medical Staff
Zimbabwe country assessment		

Organisation	Name	Role
National TB Program, MoHCC	Dr. Kavenga	Deputy Director NTP
	Dr. Manners Ncube	Technical Officer NTP
HIV/AIDS, MoHCC	Dr. T. Apolo-Mutasa	Deputy Director HIV
Department of Pharmaceutical Services, MoHCC	Mr. Gamuchirai Ngorora	Pharmacy Logistics and Research
Essential Drug List of Zimbabwe, MoHCC	Ms. Ratidzo Hove	Essential Medicines Coordinator
CHAI Zimbabwe	Mr. Kenny Sithole	Technical role not specified
WHO	Mkhokheli Ngwenya	Role not specified
Global Fund	Tari Kutadza	CCM Vice Chair
MCAZ	Dr. Pricilla Nyambayo	Not completed / no information
NATPHARM	Zisengwe	Role not specified
Zim MTech	Dr. Onai Vere	Role not specified
ZHI	Dr. Morgen Muzondo	Provincial Program Manager, Manicaland
ZNNP+	Mr. Tonderai Mwareka	Programs Officer
Union Zimbabwe Trust	Dr. Sithabiso Dube	Technical Director
ORPHID	Dr. Trudy Mhlanga	Role not specified
Jointed Hands	Melody Mukundwi	Advocacy Communication and Resource Mobilization Liaison Officer
Expert clients/caregivers, Shurugwi	Unnamed participant	Expert client / caregiver
Shurugwi District Hospital	Unnamed participant	District TB Coordinator
	Unnamed participant	TB Nurse
	Unnamed participant	TB Nurse
	Unnamed participant	Former Community Health Worker and beneficiary
Shurugwi Makusha Clinic	Unnamed participant	TB Nurse
	Unnamed participant	Facility Manager
	Unnamed participant	Environmental Health Technician
Indonesia country assessment		
WHO	Dr. Setiawan Jati Laksono	TB Representative for Indonesia
KNCV	Christiaan Mulder	Senior Epidemiologist

Organisation	Name	Role
YKI	Jhon Sugiarto	CEO
TAG	Paran Sarimitra	Technical Lead
PETA Foundation	Jumayati	Chair
Rumah Cemara	Ardhany Suryadarma	Acting Director
STPI-Penabulu	Erman Varrel	TB Specialist
REKAT - CCM	Ani Herna Sari	Director
Inisiatif Lampung Sehat (ISL) - CCM	Sudiyanto	Director
	Dian Sugianto	Manager
	Suwanah Ana	Cadre
	Khairani	Cadre
	Pristi	Cadre
	Mulat Aryani	Cadre
	Nur Intikana	Cadre
PETA Foundation	Jumayati	Chair
PR Komunitas	Dr. Betty Nababan	Executive Director
Spiritia Foundation	Daniel Marguari	CEO
Rumah Cemara	Ardhany Suryadarma	Acting Director
STPI-Penabulu	Erman Varrel	TB Specialist
REKAT - CCM	Ani Herna Sari	Director
Inisiatif Lampung Sehat (ISL) - CCM	Sudiyanto	Director
	Dian Sugianto	Manager
	Suwanah Ana	Cadre
	Khairani	Cadre
	Pristi	Cadre
	Mulat Aryani	Cadre
	Nur Intikana	Cadre
	Jumyati	Role not specified
'light touch' country assessments		
Country	Name	Organisation
India	Shamim Mannan	CHAI
Mozambique	Dr Denedita Jose	NTP
Tanzania	Lillian Mtei	KNCV
Malawi	Edna Tembo	COWLHA

APPENDIX D COUNTRY CASE STUDIES FINDINGS

This appendix presents findings from the deep-dive in-person country case studies (Cambodia, Indonesia and Zimbabwe) and light touch country assessments (Brazil, India, Malawi, Mozambique, Tanzania), as well as select findings from I4TB country closeout reports.

D.1. COUNTRY RELEVANCE AND COHERENCE

I4TB was highly responsive to country context and community priorities, demonstrating overall strong stakeholder engagement at multiple levels.

I4TB maintained good communication and coordination with NTPs/MOH, Global Fund and PEPFAR, although there were some instances of more variable coordination with other stakeholders. Across all countries included in the evaluation, strong coordination and communication was noted with NTPs/MOH and Global Fund, and where relevant, PEPFAR. I4TB supported forecasting exercises with NTPs/MOH and PEPFAR to prepare and coordinate procurement requests. The project shared data on 3HP uptake at target sites to keep national stakeholders informed. It was recognised that I4TB took care to avoid duplication of effort and leverage other donor investments to be more efficient (for example, PEPFAR's HIV care and treatment support). The project also ensured that results from clinical, programmatic and operational studies were shared in timely fashion with MOH and other key stakeholders.

“Adequate engagement was done, including periodic review sessions, update sessions, and stakeholder sessions to address concerns; they worked with MoHCC, and MoHCC was leading the implementation.” (NTP official).

In **Cambodia**, this strong coordination with National TB Programmes (NTP) and international partners was realized through a high degree of operational integration among stakeholders and multi-donor funding and technical support synergy with WHO, Global Fund, and USG.⁷¹ In **Zimbabwe**, I4TB addressed negative TPT perceptions stemming from past adverse effects with the long isoniazid regimen. The project's advocacy focused on providing evidence needed for shifting perceptions on TPT and supported government efforts to revive the confidence in TPT, shifting the narrative from risk to safety and efficacy. The project was strongly aligned with national needs by targeting high TB/HIV co-infection zones, specifically overcrowded urban areas (Harare) and artisanal mining communities (Shurugwi). In **Indonesia**, I4TB's coherence with national policy processes was demonstrated by the timely inclusion of 3HP in updated national TB and HIV guidelines and its integration into national TB and HIV information systems.

At the same time, coordination and communication with technical and implementing partners was not always as consistent at country level: while generally I4TB was thought to coordinate well with NTPs, Global Fund and USAID, in some cases, I4TB did not coordinate well with other country partners, resulting in inefficiencies, as well as concerns about mixed messages to NTPs regarding uptake of TPT regimens. *“It wasn't something that was implemented in a well-coordinated way in the country. But for us, it was a very, very good initiative.” (NTP official).*

In addition, some country level stakeholders praised I4TB's efforts to adapt tools to the local context. For example, in **Indonesia**, there was appreciation for I4TB's efforts to provide high quality translation of communication materials and to utilize culturally relevant themes in demand creation and treatment literacy activities. The importance of simple, easy to understand materials was emphasized by community partners and facilitated through materials such as TAG's guides and communication tools for advocates.

“Communities must be given more opportunities to raise awareness, using down-to-earth language rather than technical jargon. Local languages are crucial. For example[...]people mix dialects, and communication is more

⁷¹ Per description in the project's multi-partner strategy and comprehensive approach covering policy, supply and community outreach.

effective when using community language. Awareness-raising is the key thread across all TB work.” (CSO partner)

D.2. COUNTRY EFFECTIVENESS

Market-supply interventions under I4TB, including price reductions, commercialisation of FDCs and child-friendly formulations, brought tangible benefits to national TPT efforts.

“From the \$72 per patient cost down to \$15 was one of the reasons that the government eventually came to agree that we can move to shorter regimens.” (Technical partner)

Through I4TB’s market shaping work, NTPs went from having only one very expensive option in 2018 (from Sanofi) to having more affordable, quality-assured 3HP options, including an FDC to simplify administration of 3HP. Additionally, since 2024, NTPs are now able to access child-friendly, dispersible formulation of rifapentine due to I4TB’s efforts. Multiple stakeholders reported on the benefits of having more options and therefore being able to include 3HP in their national strategic plans and prepare for introduction and scale up. Specifically, it was noted that:

- In **Cambodia**, even the initial price reduction from US\$72 to US\$15 made it affordable for CENAT to maintain larger inventories than previously possible and feasible to include 3HP in their Global Fund grant.
- In **Indonesia**, I4TB was the primary driver in transitioning from 6H to 3HP, including introduction of the FDC to simplify the regimen.
- In **Tanzania**, the price reduction was a factor that helped stakeholders overcome the initial resistance of the government to include 3HP as an option for TPT among PLHIV.
- The EMAY provided an option for countries that wanted to introduce the child-friendly version of the regimen. In Cambodia, the introduction of dispersible rifapentine tablets for children was described as a “vital” innovation that addressed caregiver concerns about administration of TPT and led to improvements in treatment initiation and completion.

I4TB worked closely with the MOH, donors and technical partners to forecast and plan procurement and distribution of 3HP and 1HP. Approaches to address supply chain challenges for TPT varied across countries, including working directly with NTPs on procurement and distribution in some countries (e.g. Cambodia) and through national pharmaceutical procurement agencies in others (e.g. Zimbabwe).

Generally, the project did not directly engage supply chain partners at country level but in some cases I4TB supported distribution of 3HP to target sites in focus countries or to facilities included in operations research. The project leveraged long term PEPFAR investments in Africa, aligning TPT implementation with differentiated service delivery and multi-month dispensing to minimize the number of visits new and current PLHA on ART needed to make to receive 3HP.

In **Cambodia**, the project supported integration of the 3HP supply chain with CENAT as the central distributor and districts could request stock directly from the central level. The system was flexible to allow for moving stock within provinces to avoid shortages of 3HP. In **Indonesia**, I4TB supported early procurement through domestic budgets and donor financing, facilitated importation and distribution through special regulatory mechanisms, and strengthened coordination between national, provincial, and district levels. In **Zimbabwe** I4TB cleared the initial hurdles for importing and distributing 3HP for 20 target sites, creating a pathway nested within the routine pharmaceutical supply services that the MoHCC could follow for national scale-up. This ensured that 3HP moved through the same NatPharm provincial depots and the facility-level ordering systems as all other essential medicines. The project also improved TPT uptake and completion numbers to the National TB Program, which resulted in more accurate forecasting for ordering 3HP through the national procurement systems and reduced the procurement cycle from 6 to 3 months to ensure stable supply.

“The supply system is functioning well, and we are able to provide medicines to health centres whenever they submit requests.” (Subnational TB coordinator)

“The initial procurement for the 20 sites was done under IMPAACT4TB. Usually, there are teething problems when a new product is being introduced, but now there was already a pathway from the pilot of the 20 sites, so everything moved on well.” (NTP staff)

All countries benefitted from I4TB’s global efforts to ensure the quality of rifapentine-based TPT, including the efforts to gain WHO PQ for Lupin and MacLeods, as well as the early agreement with FHI 360 to test their products until PQ was achieved. The main challenge in terms of quality was the discovery of nitrosamine impurities in the active pharmaceutical ingredient for rifapentine, an issue that first arose for TB medications in 2020. These quality concerns delayed shipments and, in some cases, resulted in a recall of 3HP regimens that had already been delivered to focus countries.

Malawi received intensive support from I4TB to address nitrosamine contamination in batches that arrived in the country and were recalled in 2023, which caused concern among providers and PLHA. TAG developed materials to address concerns about quality concerns and the Coalition of Women Living with HIV/AIDS (COWLHA) led communication and advocacy efforts to reassure patients and providers about the process for recalling the batch and ensuring quality of the replacement. This support helped prevent a public messaging crisis that could have undermined 3HP scale up. The strong relationship with community-based organizations was central to this effort and an example of the value of partnering with trusted leaders who can advocate for 3HP at country level.

At the national level, I4TB worked with National TB and AIDS programs and advocates to update TPT clinical guidelines and trained health care providers to ensure capacity to administer and monitor 3HP, with CCSE as essential and cross cutting strategy.

In focus countries, I4TB identified existing infrastructure to leverage for 3HP introduction, which facilitated uptake by ensuring that services were provided under routine health care delivery settings. A range of capacity building activities were employed to lay the groundwork for the transition to shorter regimens, including clinical training for providers and enhancement of existing data systems to allow for pharmacovigilance and monitoring uptake and completion.

- In **Cambodia**, I4TB demonstrated that TPT could be delivered effectively through the existing health infrastructure and integrated as a routine element of care for all new PLHIV. This integration enabled 3HP to become the default rather than the exception. Between December 2020 and July 2022, a total of 834 healthcare workers from 25 provinces were trained through "Training of Trainers" (TOT) courses in **Cambodia**. This training was essential because initial scale-up of TPT for PLHIV had been slow due to staff requiring 3HP-specific clinical knowledge.
- In **Indonesia**, I4TB drove adoption of 3HP with development and dissemination of new TPT guidelines and training more than 4,000 health care providers on use of the shorter regimen. The project also used data from three pilot sites to demonstrate feasibility of 3HP implementation and advocate for implementation of the regimen.
- In **Zimbabwe**, I4TB worked directly National HIV/AIDS and TB programs to register 3HP with the regulatory authority, the Medicines Control Authority of Zimbabwe (MCAZ), a critical first step in adoption of the regimen for routine use. Registration of 3HP with MCAZ and inclusion in the National guidelines also resulted in buy-in from other donors to support procurement of 3HP for scaling-up national implementation. Successes pointed to by stakeholders included updated LTBI communication strategy, updated job aids, updated treatment algorithms, provision of training manuals, and reporting tools (all of which specify 3HP as the preferred TPT regimen).

- Although 3HP did not become available in **Tanzania** until after the first phase of I4TB was completed, evidence provided by the project was used to influence the national TPT committee's decisions about use of rifapentine-based TPT and to update country guidelines.
- **Integration considered opportunities for cost-efficiency in the patient cascade and more patient-centred approaches:** In **Zimbabwe**, I4TB's efforts to align TPT and ART services created efficiencies that made 3HP more affordable than 6H in terms of costs to the health system. This "one stop shop" model also reduced the time spent by PLHA in accessing care. The minimal side effects also reduced the number of visits and time spent by providers managing clinical care. In **Tanzania**, one interviewee reflected that leveraging the HIV program's differentiated service delivery model to provide 3HP saved health system and patient costs associated with the 6-month regimen of isoniazid.

At the same time, there were barriers to country level adoption that were not successfully addressed. For example, in **South Africa**, where DOLPHIN and other research studies were undertaken that influenced uptake across the world, the MOH has still not approved a child-friendly formulation of rifapentine.

A strength of I4TB was working with civil society and community-based organizations to advocate for adoption of TPT in NTP guidelines, improve treatment literacy among the population and address bottlenecks in implementation of rifapentine-based regimens. TAG provided training in treatment literacy and developed resources to support civil society and community-based organizations to advocate for the shorter rifapentine-based regimens, including *An Activist's Guide to Rifapentine TB Preventive Treatment*.

"Initially, some clients were hesitant to collect 3HP, fearing side effects based on the INH experiences, but with Expert clients sharing their experiences with 3HP during community support groups, this helped to alleviate these fears and increased uptake of 3HP." (CSO partner)

- In **Malawi**, treatment literacy campaigns were implemented to create demand the shorter 3HP among PLHA. COWLHA developed a treatment literacy curriculum and trained a network of "expert women" to lead education sessions on TPT in facilities, churches and marketplaces. This CSO's long standing reputation as a trusted resource for women living with HIV/AIDS was critical to the success in advocating for TPT among communities throughout Malawi. In addition to the structured treatment literacy sessions, they visited households and markets to bring information to community members in less formal ways.
- I4TB used an innovative testimonial approach to reassure PLHA that 3HP was safe in **Zimbabwe**, where there was an existing fear of TPT due to negative experiences with side effects associated with the 6H regimen. Expert clients shared their experiences with 3HP at community support groups for PLHA to counter negative information about TPT that was discouraging uptake.
- The contribution of community-based organizations to creating demand and supporting adoption is also illustrated by the experience in **Cambodia**. When qualitative research revealed that social stigma remained a pervasive barrier to uptake, KHANA and Cambodia Health Committee mobilized right-based advocacy activities by supporting contact investigation and framing TPT as a right for contacts and an important health service for the community. They led screening and education sessions, including in pagodas, to spread correct information about TPT.

Engagement of civil society and collaboration with community-based organizations was an essential and cross cutting project strategy. Without these partnerships, it would have been more difficult to address the barriers Unitaids sought to overcome.

I4TB collaborated with trusted partners to advocate for rifapentine-based TPT at national and community level, with specific activities aimed at reaching key policy and program officials, as well as health care providers, PLHA and contacts of people with TB. Civil society actors were "at the table" in several countries as guidelines were being developed and/or adapted.

- The Zimbabwean National Network of People Living with HIV (ZNNP+) and Jointed Hands Welfare Organization were highly effective in **Zimbabwe** because they utilized long-standing, well known structures to conduct advocacy at all levels. Since PLHIV are the largest TPT client group, these CSOs were uniquely positioned to create "bottom-up" demand through treatment literacy. Both CSOs were grantees of the TAG small grants and worked together with CHAI and MoHCC to develop tools for community engagement and advocacy activities. Stakeholders used a mix of traditional community meetings and social media/online platforms to raise awareness and ensure 3HP responded directly to patient needs for reduced side effects and shorter treatment duration.
- In **Cambodia**, Partnerships with CSOs such as KHANA and CHC were critical in building the community-level conditions necessary for scale-up, often filling operational capacity gaps that the government's limited budget could not cover. For example, they assisted with contact investigation and adherence monitoring and conducted campaigns to raise awareness about TPT. Additionally, community health workers played a vital role in mitigating social stigma and discrimination, which are primary hindrances to treatment adoption.
- In **Indonesia**, the role of civil society and community-based organizations in supporting new TPT regimens was more limited. They were active in demand creation and provided adherence support but were not as involved in national level in policy issues or national strategic planning. This was viewed as a missed opportunity to strengthen TPT services and enhance sustainability.

Additionally, I4TB had to rethink the role of CSOs and CBOs in cases where the MOH and civil society did not have a strong relationship. For example, a strategy to engage patient advocates with the MOH backfired in one country, where the government believed advocates were being paid to influence policy. I4TB stepped back and supported the country by advocating for and supporting a TPT technical committee to provide relevant and transparent information on 3HP, which eventually led to its adoption in MOH guidelines.

"It was mostly through persistence... requesting for meetings and meeting with people who were changing the policy, and also the introduction of this particular committee, which was formed by the ministry, but through persuasion from the IMPAACT4TB." (Implementing partner)

The timing and intensity of civil society involvement varied by country; some stakeholders reported being present from the initial I4TB activities in country, while others noted that they were involved later in implementation and felt that it would have been beneficial to be brought in earlier in the process of developing TPT policies and guidelines. And while civil society organizations were clearly valued, the amount of funding provided by I4TB as a percentage of their overall budget was very small (about 1%). The one-year funding cycle also limited the long-term impact of civil society and community-based partners funded through the small grant program. The short duration of activities did not allow for sustained momentum of results or maintenance of relationships with policymakers and other key stakeholders.

By engaging civil society partners and community-based organizations, I4TB was very effective in creating demand for rifapentine-based TPT among PLHIV and providers.

Through efforts of civil society, training of health care workers and dissemination of critical research findings at global and country level, I4TB dispelled myths about TPT and encourage uptake of rifapentine-based treatment among PLHA. Demand creation was more challenging for household contacts, but having a shorter regimen with fewer side effects encouraged uptake. Risks and benefits are clear, and contacts who do not feel sick are more likely to take and adhere to the shorter regimens. Civil society actors were enlisted to address a range of misconceptions and other communication challenges.

"Community members often questioned: 'Why should I take medicine if I'm not sick?' In addition, discrepancies in drug allocation created confusion. For example, some patients received a 3-month regimen, others 6 months, leading to perceptions of unfairness." (Civil society partner)

The successful demand creation was not always aligned with efforts to ensure a reliable supply of 3HP. There were multiple challenges with delayed registration and shipments in some countries, and it is important to reflect on the timing of these activities and whether they should be more carefully planned.

I4TB also supported implementation and evaluation of service delivery models aimed at optimizing uptake of TPT among PLHIV and child contacts. In focus countries, the project provided practical support to adapt TPT service delivery tools (for example job aids, communication aids for health care providers, training manuals and reporting forms) to facilitate uptake of rifapentine-based TPT at all levels of the health system.

- **Zimbabwe** was included in the multi-country OPT4TPT study funded by the Bill and Melinda Gates Foundation in partnership with I4TB, which assessed uptake and completion of 6H and 3HP, including frequency of adverse events and gaps in provider adherence to guidelines and recommended prescription practices.
- Partners in **Cambodia** decentralized distribution of 3HP, utilizing teams to bring medication directly to households to reduce geographic barriers to care.
- I4TB implemented the CHIP study, a multi-method research study to compare community-based initiation of TPT to facility-based services in **Ethiopia** and provided data to support the refinement of TPT delivery in different geographic and clinical settings. The project drew on similar service delivery research undertaken by CaP-TB to identify the most effective approaches for delivering 3HP in Cameroon and Uganda.

Many of I4TB's civil society partners were affected by the 2025 dismantling of USAID and is not clear to what extent some of these innovative models continue.

D.3. COUNTRY SCALABILITY, IMPACT AND SUSTAINABILITY

I4TB achieved high TPT coverage among PLHIV through integration with existing systems, though impact among household contacts and long-term sustainability remain constrained by weak contact investigation and reduced TB financing.

I4TB laid the groundwork for scale up with the following aspects being described as being particularly valuable: (1) supporting countries to adopt rifapentine-based TPT into national policies and guidelines, (2) training of health care providers on determination of eligibility for and administration of TPT, (3) community engagement to create demand for TPT and implementation research to identify promising models for service delivery.

In **Cambodia**, I4TB contributed to creating the conditions for TPT scale up with a wide range of interventions, including engagement of community-based organizations to create demand for TPT, training providers, implementing contact investigation and monitoring adherence. In **Indonesia**, I4TB worked with MOH officials to include 3HP in the National TB Strategic Plan and TPT guidelines, an important pre-condition for scale up. Scale up has been uneven due to gaps in the availability of 3HP and suboptimal demand, which suggests that the demand creation activities were not as effective in Indonesia as in other countries. In **Zimbabwe**, I4TB embedded activities within national structures rather than building parallel systems and ensured that lessons learned from the initial 20 target sites were used to inform scale up. The project also advocated at national level to include 3HP in the essential medicines list and shift official TPT policy to 3HP, which was a critical step for getting buy in and nationwide acceptance of the regimen among providers. Refer to Appendix H.3 for further information on scale of TPT across the 12 I4TB countries over 2020-2024, based on the latest WHO reporting.

Although I4TB procured initial batches of rifapentine-based TPT as national TB programs introduced and rolled out new regimens, several countries moved quickly to assume the cost of procurement and distribution of adult formulations.

I4TB supported the first procurement of rifapentine-based TPT in **Cambodia** in 2021, transitioning from loose tablets to the FDC in the scale up phase. By 2024, the government had committed to covering procurement costs for all adult TB medications, an important step towards sustainability. In 2022, the National TB Program in **Indonesia** planned to procure rifapentine (150 mg) and isoniazid (300 mg) tablets with domestic resources. They also included 3HP FDC in their Global Fund budget. The National AIDS Program has planned to procure 10,000 doses of 3HP FDC for PLHIV also with funding from Global Fund. **Zimbabwe** faces challenges with limited funding for TB overall. There was a sharp decline in the total basket of funding for TB from US\$ 20.1 million in 2022 to US\$ 6.8 million in 2024 with international funding reducing significantly from US\$ 19.3 million to US\$ 6.8 million during this period.

I4TB was an important partner in supporting countries to reach their UNHLM commitments on TPT made in 2018, particularly for PLHIV. The project is credited with making a significant contribution to reducing morbidity and mortality due to TB by increasing coverage of TPT.

In addition to epidemiological impact, I4TB was noted for its contribution to improvements in health system efficiency with the shorter regimen, increased adherence and efforts to reach vulnerable populations in **Cambodia**, where TPT completion has reached 98-100% in some cohorts and treatment abandonment is almost non-existent. One stakeholder noted that the project built the “very strong will” of the national government to accelerate TB elimination. Highlighting community-level success, local health centre staff noted that *“the most notable impacts include a noticeable reduction in new TB cases and increased community awareness regarding prevention.”* Similar observations were made in **Zimbabwe**, where the transition to 3HP resulted in fewer tablets dispensed, simplified stock management, and a reduced burden on healthcare workers regarding the tracking of adverse drug events, as well as an assumed effect on incidence due to higher TPT coverage and completion rates. While it is too soon to assess impact in **Tanzania**, TPT initiation among PLHIV has increased as 6H has been phased out and 3HP replaced it.

While the current funding crisis has created uncertainty regarding future funding, I4TB’s work at country level provided a strong foundation for sustainability.

For example, except for research studies and some enhanced M&E for pilot sites, I4TB largely worked with the national TB and HIV data systems in country and avoided setting up siloed data collection activities. They integrated the key TPT indicators needed to monitor uptake and completion of TPT with existing reporting activities rather than collecting data in parallel reports, thus aiding sustainability. In **Cambodia**, TPT data is recorded and reported through the national TB reporting system managed by CENAT. CHAI worked with CENAT to integrate data points needed for routine monitoring of TPT implementation into this system. The national TB and HIV systems in **Indonesia** (SITB and SIHA) capture information from patient records that is used to create cohort analysis to monitor uptake and completion of TPT. In **Zimbabwe**, I4TB supported the NTP to improve availability and quality of data in the existing DHIS2 system, which was linked to the logistics management information system (LMIS) to ensure accurate quantification and distribution of 3HP.

APPENDIX E I4TB STUDIES AND IMPACT ON POLICY

Table Figure E. 1 below summarises the key sources identified by Unitaid and Aurum as having contributed to policy impact under the grant. It sets out the evidence or technical input generated by each source and, where relevant, the WHO guidelines, recommendations or policy processes that this work informed.

Figure E. 1: Key studies, evidence generated and policy impacts from the I4TB grant

Study name	Evidence generated	Key policy impact (if applicable)
Safety and pharmacokinetic		
DOLPHIN One	3HP can be given with once-daily DTG-based ART in virologically suppressed PLHIV, with no DTG dose adjustment required. Link	WHO TPT 2020 guideline expansion
DOLPHIN Too	3HP and DTG-based ART can be started simultaneously in ART-naive PLHIV, with viral suppression maintained and no DTG dose adjustment required. Link	WHO TPT 2020 guideline expansion
TBTC 35 Pediatric Dose Study	3HP was safe and well tolerated in children, with trial-based weight-banded dosing supporting use in young children, including those under two years and those with HIV. Link	WHO TPT 2024 guidelines on peds dosing
Dolphin Kids (3HP in Children HIV on DTG)	3HP can be co-administered safely with DTG-based ART in ART-experienced children with HIV weighing at least 10 kg, without DTG dose adjustment but with strong adherence support. Link	WHO HIV treatment guidelines 2025
Dolphin Moms (1HP and 3HP in pregnant WHIV on TLD)	3HP can be used safely in pregnant women with HIV on once-daily DTG-based ART, with therapeutic DTG levels and viral suppression maintained, supporting guideline expansion. Link	WHO HIV treatment guidelines 2025
One to Three (1HP vs 3HP)	1HP and 3HP are safe TB prevention options for adults with or without HIV, offering patient choice and programme flexibility, although 1HP had more treatment-limiting adverse events and lower composite completion. Link	WHO HIV treatment guidelines 2025
Enhanced M&E	3HP was highly acceptable and well tolerated in children with HIV and child household contacts, with high completion, no discontinuations due to adverse events and no TB cases during follow-up. Link	WHO TPT 2024 guidelines, reinforcing 3HP; 2025 HIV testosterone replacement therapy (trt) guidelines
Implementation science		
Choice Architecture study (CAT-Study)	Default TPT prescribing did not consistently improve prescribing across countries, highlighting the need for further innovation to ensure people	WHO HIV treatment guidelines 2025 (+ upcoming)

Study name	Evidence generated	Key policy impact (if applicable)
	starting ART receive appropriate TB prevention or treatment. Link	
CHIP-TB study	Home-based child TB contact tracing and TPT provision can improve access and acceptability without increasing societal costs, but should be supported by task-sharing and active community engagement. Link	Country use to guide national planning (2024)
CUT-TB study	The evidence generated is not publicly available. The trial aimed to generate evidence on whether more intensive TB testing among contacts improves case finding and cost-effectiveness in high-burden settings, where costs and delivery conditions differ from lower-burden contexts. Link	N/A
Opt4TPT	Qualitative findings highlight modifiable clinic- and community-level barriers to TPT initiation and completion among PLHIV, including side effects, pill burden, drug interaction concerns, healthcare experiences and stigma. Link	N/A
CRUSH — Crushed Tablet Trial	The CRUSH Study supports breaking or crushing rifapentine formulations for children, while EMAV implementation will provide practical insights on paediatric 3HP delivery and dosing. Link	WHO TPT 2024 guidelines on peds dosing (2023 data)
Cost effectiveness		
Cost-effectiveness of 3HP	Cost-effectiveness evidence should inform TPT planning and scale-up, recognising that value for money will vary by local systems, TB prevalence and patient preferences. Link	Lancet article; WHO TPT 2024 guidelines; 2025 HIV treatment guidelines
Reviews		
Tuberculosis Preventive Treatment in High TB-Burden Settings: A State-of-the-Art Review	Recent advances in diagnostics, shorter TPT regimens, child-friendly formulations and lower prices support cost-effective global scale-up, but major delivery gaps remain for child and household contacts. Link	N/A
Other		
Guidance on evidence generation on new regimens for tuberculosis preventive treatment	Set out the evidence requirements for assessing new TPT regimens, including data on efficacy, safety, adherence, feasibility, acceptability and programmatic implementation. It did not generate new trial evidence, but helped define the evidence pathway for future TPT regimen development. Link	Supported WHO's research and innovation agenda for new TPT regimens, rather than directly informing a specific treatment recommendation.

APPENDIX F TPT SCALE-UP AND FINANCING

This appendix assesses the I4TB contribution to global uptake of TPT, overall global progress, and available country coverage and financing data, as reported to WHO. It includes the following analysis:

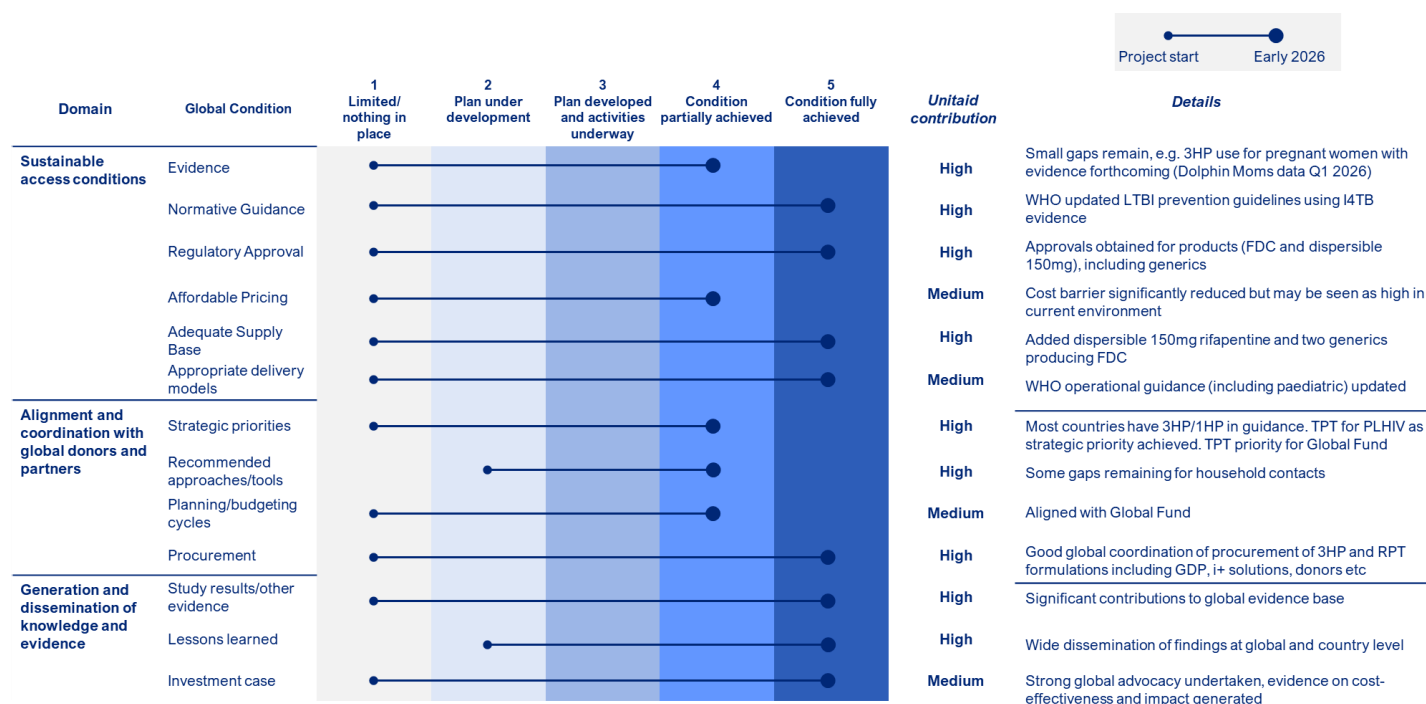
- Unitaidd global scalability matrix (F.1)
- Trends in global TPT coverage against 2027 global goal for priority populations (F.2)
- Scale of 3HP among PLHIV and household contacts across the 12 I4TB countries (F.3)
- Analysis of TPT country funding for I4TB countries (F.4)

F.1. UNITAID GLOBAL CONDITIONS FOR SCALE

Figure F.1 assesses the global conditions for scale up of TPT and Unitaidd's contribution to those conditions. Overall, the evidence suggests two key points:

- Strong progress has been made and Unitaidd/ I4TB's contribution has been highly significant. This contribution has often been amplified through effective partnerships with other organisations, for example where affordable pricing conditions were secured through coordinated market-shaping efforts.
- For 'Alignment and coordination with global donors and partners', we note the recent 2025 funding crisis as a risk, not on the efforts and achievements of the project.

Figure F.1 Global conditions for scale up and Unitaidd contribution⁷²



Source: CEPA analysis of data provided by Aurum and Unitaidd

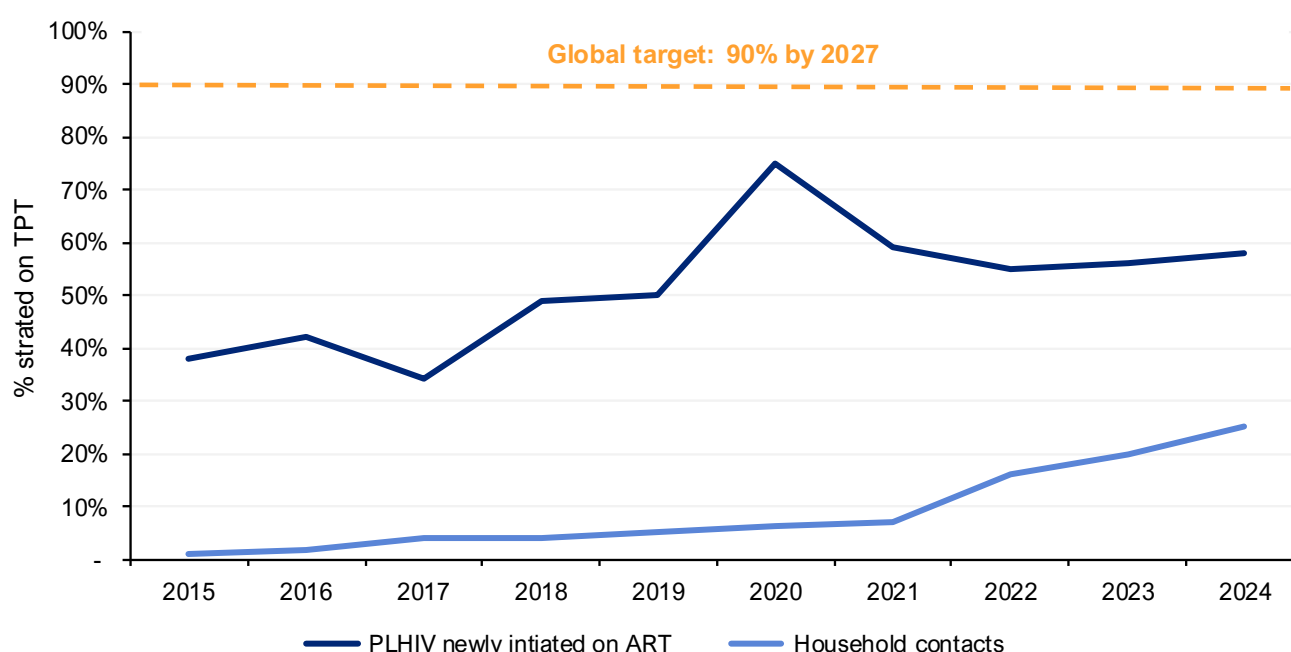
⁷² Project start scoring and initial perception of progress achieved by early 2025 as per Unitaidd Scalability Framework March 2023 as filled in by Aurum. Some adjustments to progress achieved and details is CEPA analysis.

F.2. GLOBAL COVERAGE OF TPT

Global TPT coverage has increased, but current volumes remain materially below the level required to meet the 2023-27 target. The 2023 UN high-level meeting on TB set a new global target of 90% TPT coverage among people at high risk of developing TB. This is equivalent to providing TPT to approximately 45 million people globally over 2023-2027, including around 30 million household contacts of people with TB and 15 million people living with HIV.⁷³

Figure F.2 shows a positive global trend in TPT coverage for household contacts, and a ‘re-leveilling’ of coverage for PLHIV following a peak in 2020. This suggests that global TPT has made progress, but not at the pace required to reach the targets, and the major efforts to enrol PLHIV on TPT were not sustained at the same intensity. The gap is particularly large for household contacts. Achieving the target will require a substantial acceleration in TPT initiation alongside other factors.

Figure F.2: Global coverage of TPT



Source: CEPA analysis of WHO's Global tuberculosis report 2025⁷⁴

F.3. SCALE OF 3HP IN I4TB COUNTRIES 2020-2025

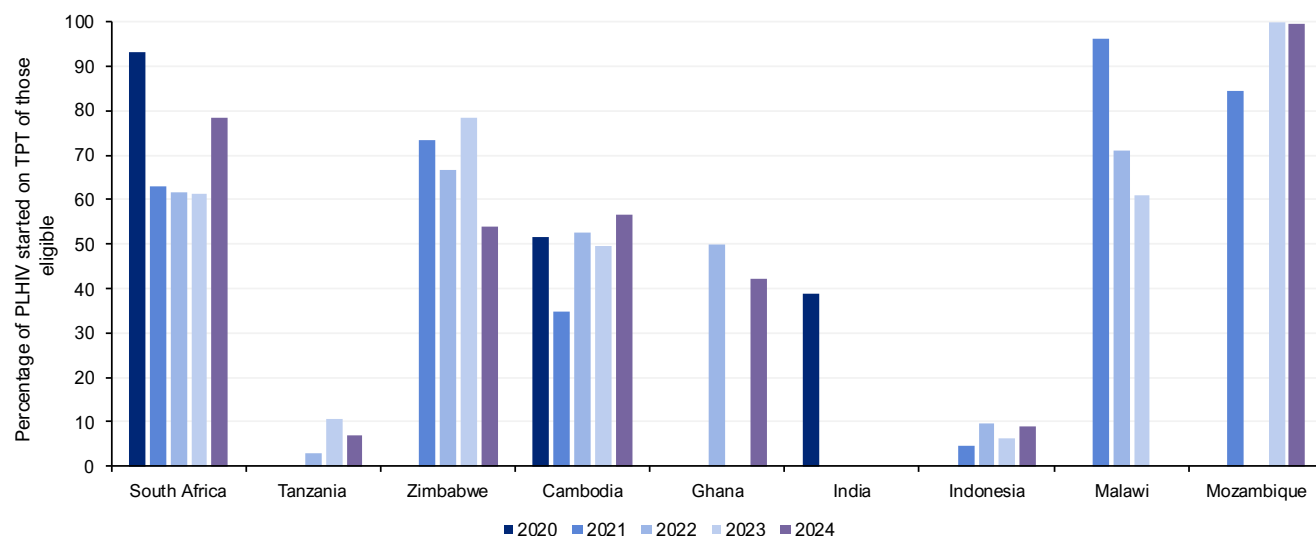
Figures F.3 and F.4 provide TPT coverage among PLHIV and household contacts in the 12 I4TB project countries over 2020-2025, as reported to WHO (only reporting countries shown). Coverage is higher among PLHIV than among household contacts, although performance varies across countries over time.

Among PLHIV, TPT initiation was generally high in the most recent year, with coverage above 50% in most countries. However, trends over time are mixed: some countries have improved coverage, while others have seen weaker performance. This suggests progress has not been uniform and is dependent on country specific factors.

⁷³ WHO (2025), Global Tuberculosis Report 2025

⁷⁴ WHO (2025), Global tuberculosis report 2025

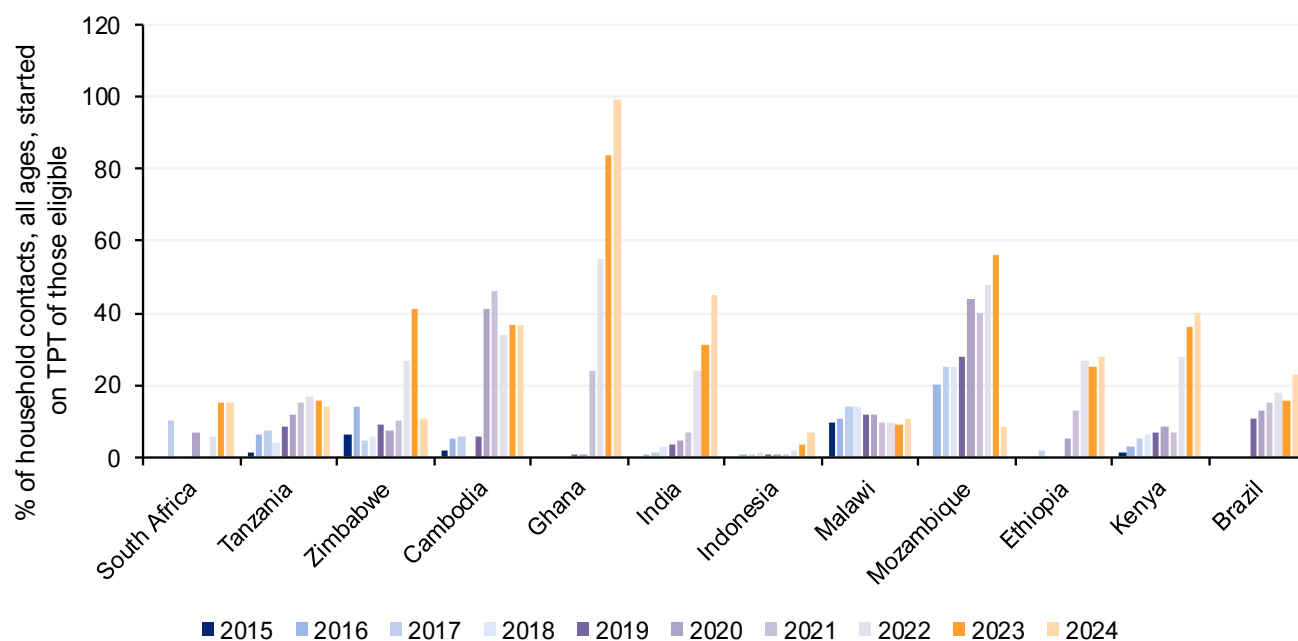
Figure F.3: Percentage of people living with HIV who were started on TPT out of those eligible in I4TB project countries 2020-25 (reporting countries only)



Source: CEPA analysis of WHO's Global tuberculosis Dashboard.⁷⁵

Coverage among household contacts has increased in most I4TB countries, with particularly strong progress in Ghana and Mozambique. However, overall coverage remains lower for household contacts than for PLHIV coverage overall.

Figure F.4: Percentage of household contacts (or all close contacts) of all ages who were started on TPT out of those eligible in I4TB project countries 2020-2025 (reporting countries only)



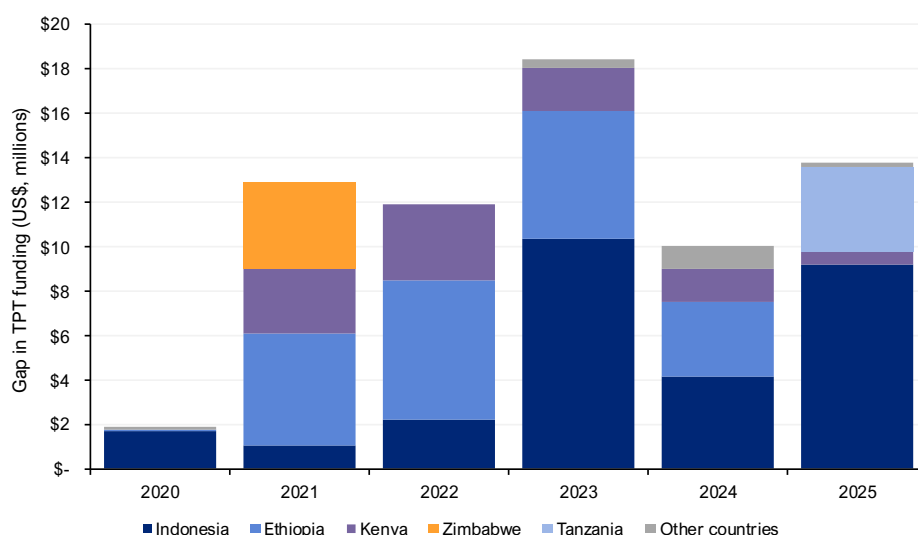
Source: CEPA analysis of WHO's Global tuberculosis Dashboard.

⁷⁵ Global Programme on Tuberculosis & Lung Health. Available at: <https://data.who.int/dashboards/tuberculosis?m49=004> (Accessed 12 June 2026).

F.4. ANALYSIS OF TB FUNDING

There are concerns on the impact on TPT given the reduced global financing available. However, the data is limited so far, as shown in Figure F.5. Out of the 12 I4TB countries, only four have provided substantive funding data for 2025. Brazil, India, Mozambique and South Africa are not represented below as they did not report any gaps in TPT funding between 2022 and 2025.

Figure F.5: Gap between the funding required and funding available for prevention treatment, 2020-2025⁷⁶



Source: CEPA analysis of WHO's Global tuberculosis Dashboard.

⁷⁶ Other countries include Ghana, Malawi and Cambodia.

APPENDIX G MARKET SHAPING INSTRUMENTS

Table G.1 describes the market shaping tools used in the project and their application.

Table G.1: IMPAACT4TB Market shaping tools and their application

Market shaping intervention	Rationale and expected benefits	IMPAACT4TB application
Adjustable purchase order	Creates a credible demand signal by committing to future purchases while allowing actual procurement by eligible buyers to count toward the commitment. Reduces demand uncertainty, incentivizes manufacturer investment, and supports lower pricing without requiring upfront guarantee capital.	IMPAACT4TB adapted a traditional advanced purchase commitment into an adjustable purchase order with Sanofi, under which purchases by eligible procurers counted toward the committed volume over a defined period. Combined with catalytic procurement and coordinated buying, this provided the credible demand signal Sanofi needed to invest in production for an unproven LMIC market, while avoiding displacement of routine procurement or the need for upfront guarantor capital.
Catalytic procurement	Uses early purchases to stimulate commercial production, introduce new products, or bridge temporary procurement financing delays. Reduces manufacturer timing risk and accelerates product availability and adoption.	IMPAACT4TB procured initial commercial volumes of Sanofi rifapentine to encourage manufacturers to produce commercial batches and support early product introduction while routine procurement mechanisms developed. This was considered an appropriate complement to the adjustable purchase order because manufacturers remained hesitant to invest before the market had matured. (Where countries lacked the enabling environment for adoption rather than financing, the EMAB was used instead, as for pediatric rifapentine)
Coordinated buying (pooled procurement)	Aggregates demand across multiple purchasers while allowing each to retain its own procurement policies. Improves supply planning, increases purchasing power, reduces stockout risk, and supports equitable allocation.	IMPAACT4TB coordinated procurement planning among major procurers—including the Global Fund, PAHO, PEPFAR, and South Africa—through joint forecasting and regular engagement with manufacturers. This approach was selected because demand was fragmented across several buyers, none of whom individually could justify manufacturer investment. Coordinated purchasing created a sufficiently strong aggregate demand signal while improving supply planning and equitable allocation.
Development/commercialization cost offset grant	Offsets fixed development or commercialization costs that keep prices above affordable levels. Enables lower launch prices in exchange for binding access commitments on affordability, quality, and availability.	IMPAACT4TB provided grant funding to offset Macleods' and Lupin's market entry and commercialization costs where fixed investment was preventing achievement of the target price. This approach was pursued because reducing fixed costs enabled lower prices without distorting long-term production economics, while legally binding access conditions ensured public benefit.
Volume guarantee (VG) - risk-adjusted, capped	Guarantees a minimum purchase volume in exchange for price and capacity commitments, reducing commercial risk	IMPAACT4TB collaborated with MedAccess to implement a volume guarantee with Macleods, backed by MedAccess as independent guarantor for

Market shaping intervention	Rationale and expected benefits	IMPAACT4TB application
maximum risk value	associated with expanding production. Supports rapid scale-up and lower prices while limiting financial exposure through capped guarantees.	the largest generic formulation, where production capacity needed to increase nearly eightfold from a very small production base. This was the appropriate tool to continue to support more affordable 3HP: guaranteeing demand reduced manufacturer risk, unlocked capacity expansion, and secured lower prices while capping MedAccess' financial exposure.
Co-payment	Provides an upfront payment that bridges the difference between higher unit costs at low production volumes and lower costs achieved at scale. Allows affordable pricing from market launch.	IMPAACT4TB provided a co-payment to bridge the gap between manufacturers' higher initial production costs and lower costs achievable once volumes increased. This approach was chosen because production costs naturally declined with scale; the co-payment enabled countries to access the target price immediately instead of waiting for market volumes to grow.
Early Market Access Vehicle (EMAV)	Uses conditional purchase commitments tied to manufacturer access commitments and country readiness. Accelerates product introduction while encouraging sustainable market development and avoiding dependence on donor-funded procurement.	IMPAACT4TB deployed the EMAV for Lupin's rifapentine 150 mg dispersible formulation. Purchase commitments were contingent on the manufacturer's meeting access commitments and countries establishing the necessary policy and implementation environment. This was preferred over catalytic procurement or unconditional donations because it linked early access to measurable progress toward sustainable market entry rather than creating open-ended donor dependence.
Standard competitive procurement tender	Appropriate once a competitive, sustainable market with multiple suppliers has been established. Maintains affordable pricing and reliable supply through routine market competition.	Once multiple suppliers had entered the market and competition had been established, the Global Drug Facility transitioned procurement to standard competitive tenders, coordinated with other procurers. This was considered the appropriate end-state because the market no longer required active shaping interventions and could sustain affordability and reliable supply through normal competitive procurement.



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