



MARCH 2017

South Africa Needs Assessment for Optimized Antiretroviral Drugs and Regimens

TABLE OF CONTENTS

INTRODUCTION

- 02 — Abbreviations
- 02 — Purpose
- 03 — Country Context
- 04 — Methods
- 05 — Operational Framework

FINDINGS

- 06 — Domain 1: Enabling environment (policy, advocacy, and finance)
- 08 — Domain 2: Planning processes and tools
- 09 — Domain 3: Service delivery capacity
- 10 — Domain 4: Transition monitoring and visibility

ANNEX

- 14 — Appendix 1: List of Interviewees
- 15 — Appendix 2: Interview Guide

SUMMARY

- 11 — Summary of Findings
- 12 — Illustrative Product Introduction Work Plan: South Africa

Purpose

The aim of the **OPTIMIZE** Consortium¹ is to accelerate the development, testing, and market introduction of optimized antiretroviral (ARV) products to support the best possible treatment outcomes for people living with HIV in low- and middle-income countries (LMIC). Optimized ARV products are those that are 1) effective, safe, well-tolerated, and easy to use for LMIC priority populations (including children, pregnant women, and TB patients), and 2) adapted to resource- and infrastructure-constrained environments (i.e. affordable, heat-stable, and available in fixed-dose combinations [FDC]). Optimization offers extensive health benefits, including improved adherence and decreased treatment failure due to higher tolerability, lower toxicity, reduced drug resistance, and fewer side effects; increased patient compliance thanks to smaller tablet sizes; and decreased HIV transmission and incidence as a result of earlier and more sustained viral suppression.

The optimization process consists of a combination of global interventions to bring optimized ARV products to market rapidly and local preparations to ensure they reach patients in LMIC efficiently and effectively. At the local level, some past transitions to new ARV products have been hindered by issues such as national policy and regulatory barriers, tendering and procurement challenges, supply chain interruptions, slow uptake by prescribers, and patient apprehension. To avoid these and other stumbling blocks during the transition to optimized ARV products containing dolutegravir (DTG) and tenofovir alafenamide fumarate (TAF) in the next two to three years, countries must understand their capacity and readiness in key domains relating to new product introduction.

The **OPTIMIZE** Country Needs Assessment assesses national capacity and readiness across four functional domains: 1) Policy, Advocacy, and Finance; 2) Planning Processes and Tools; 3) Service Delivery Capacity; and 4) Transition Monitoring and Visibility. Drawing on quantitative and qualitative data, the Assessment assigns a “need rating” of low, moderate, or high to each of four sub-domains and identifies priority bottlenecks or weaknesses where action is required to ensure that the transition to a DTG-containing FDC (from Tenofovir/Lamivudine or Emtricitabine/Efavirenz [TLE]) commonly referred to as TLD and other optimized products maximizes health and budgetary benefits.

ABBREVIATIONS

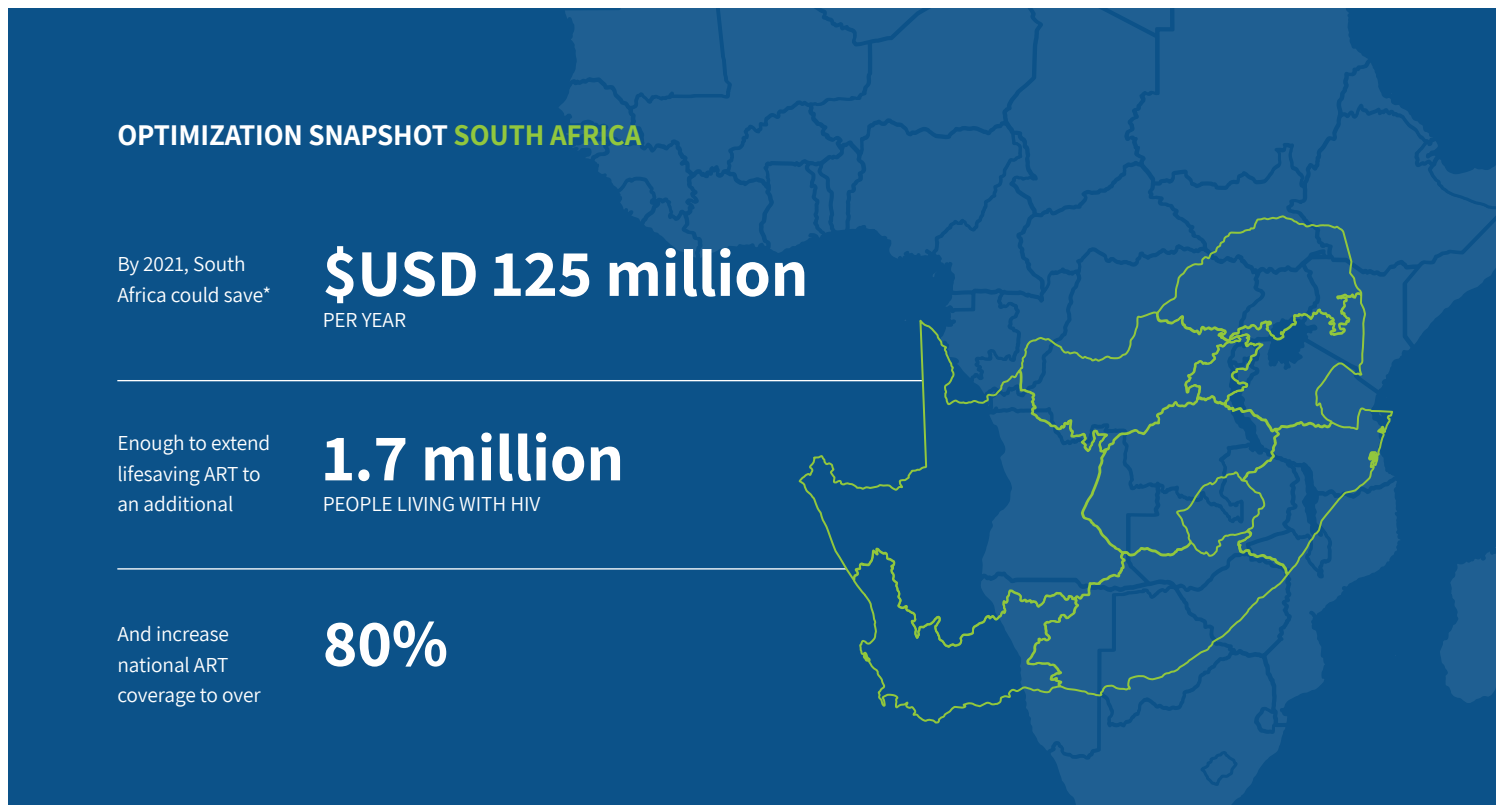
ARV	Antiretroviral (drug)	FTC	Emtricitabine	SAHPRA	South African Health Products Regulatory Authority
ART	Antiretroviral therapy	GFATM	Global Fund to Fight AIDS, TB, and Malaria	SOP	Standard Operating Procedure
BMGF	Bill and Melinda Gates Foundation	HIV	Human immunodeficiency virus	SPP	Stop Stockouts Project
CDC	Centers for Disease Control and Prevention	LMIC	Low and/or Middle Income Countries	TAC	Treatment Action Campaign
CHAI	Clinton Health Access Initiative	LPV/r	Lopinavir/ritonavir	TAF	Tenofovir alafenamide fumarate
d4T	Stavudine	M&E	Monitoring and Evaluation	TAFxDTG	Tenofovir alafenamide fumarate/Lamivudine or Emtricitabine/Dolutegravir
DCGI	Drug Controller General of India	MCC	Medicines Control Council	TLE	Tenofovir/Lamivudine or Emtricitabine/Efavirenz
DFID	Department for International Development	MSF	Médecins Sans Frontières	USAID	United States Agency for International Development
DTG	Dolutegravir	NDRRA	National Drug Regulatory Authority	USG	United States Government
DRV/r	Darunavir/ritonavir	NDOH	National Department of Health	VL	Viral Load
EFV400	Efavirenz 400	PEPFAR	President's Emergency Plan for AIDS Relief	WHO	World Health Organization
EMR	Electronic Medical Record	RuDASA	Rural Doctors Association of Southern Africa		
ePTS	Electronic Patient Tracking System	SAG	South African Government		
FDA	Food and Drug Administration	SAHCS	Southern Africa HIV Clinicians Society		
FDC	Fixed-dose combination				

1. The founding members of the consortium include: (1) Wits Reproductive Health and HIV Institute, with expertise in research, program implementation, policy, and training; (2) ICAP at Columbia University, with extensive experience providing site-level, sub-national, and national support to scale up and increase quality of HIV services; (3) Mylan Laboratories Limited, a global generic and specialty pharmaceuticals company; (4) the University of Liverpool, with unique capabilities in Solid Drug Nanoparticle technology; and (5) the Medicines Patent Pool, a United Nations-backed not-for-profit organization that secures lower pricing for HIV medicines through voluntary licensing and patent pooling.

Country Context

With 3.4 million people receiving ART in 2016, the **Republic of South Africa (RSA)** is home to the world's largest antiretroviral therapy (ART) program. Since adopting the World Health Organization's "Treat All" recommendation in September 2016, the number of people living with HIV eligible for ART in RSA has grown to nearly seven million. Providing the current ART regimens to all people living with HIV would require additional funding of up to USD \$300 million annually² and would impose a significant strain on the resources of the Government of South Africa, which currently funds 91 percent of ARV drugs purchased. By rapidly adopting and scaling up optimized ARV products – particularly an FDC containing DTG and TAF – RSA could realize estimated annual per patient per year (pppy) savings of up to USD \$41 by 2021, and total annual savings of more than USD \$125 million.* Savings will continue to grow as optimized ARVs achieve economies of scale.

THE NUMBER OF PEOPLE LIVING WITH HIV ELIGIBLE FOR ART IN RSA HAS GROWN TO NEARLY 7 MILLION.



* Calculation based on estimated savings from switching from TLE to TLD for as the preferred 1L regimen using the estimated market introduction price for TLD of \$75 pppy and RSA 2015-2018 tender weighted average price for TLE based on the CHAI ARV Market Report 2016 and estimated average of patients on ART between 2017 and 2021.

2. Based on 2016 expenditure for ARV drugs cited in PEPFAR COP SDS for 2016.

Methods

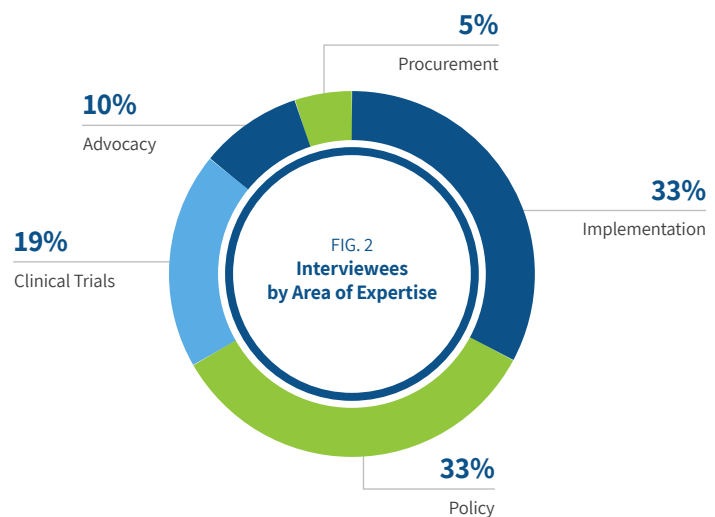
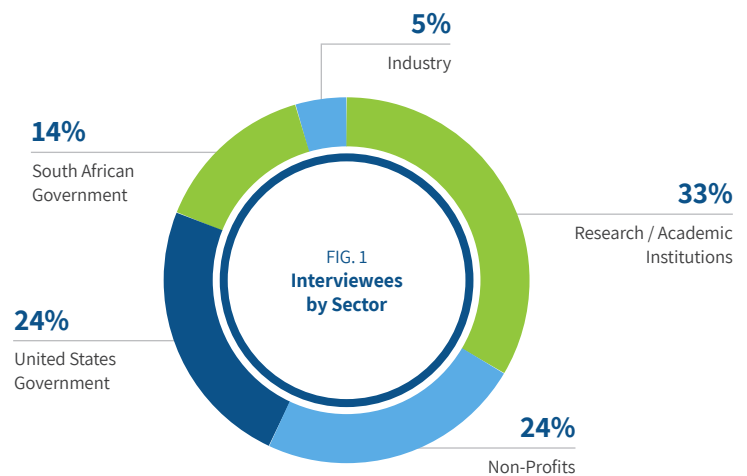
DESK REVIEW:

Much of the contextual and quantitative data for the needs assessment was drawn from relevant reports and other literature, including peer-reviewed journals, official government announcements, and popular media coverage.

KEY INFORMANT INTERVIEWS:

Interviews were conducted from September 12 to September 23, 2016. Interviews were held in-person in Johannesburg and Pretoria with the exception of two telephonic conversations with stakeholders located in Durban and Cape Town. Interviews were recorded and ranged in length from 30 to 60 minutes, with the vast majority of the latter duration.

Twenty-one interviews were conducted with respondents representing a wide range of sectors (Figure 1), and areas of expertise (Figure 2). The full list of interviewees can be found in Appendix 1.



Operational Framework

This assessment is structured around four functional domains of product introduction and scale-up that were identified as strongly influencing the organization and success of past ARV transitions, based on input from multiple stakeholders consulted for a stakeholder landscape analysis, which **OPTIMIZE** conducted in 2016.



DOMAIN 1

ENABLING ENVIRONMENT (POLICY, ADVOCACY, AND FINANCE)

Are national policies, advocacy platforms, and financial processes ready to facilitate new product introduction?



DOMAIN 2

PLANNING PROCESS AND TOOLS

Do tools and processes for forecasting, tendering, target-setting, and transition monitoring require updating or adaptation?



DOMAIN 3

SERVICE DELIVERY CAPACITY

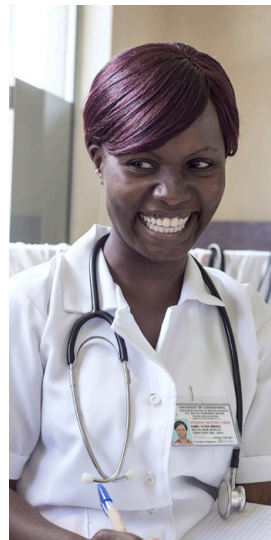
Are ART service delivery models and health care workers prepared to support the introduction of new ARV products and enhanced patient monitoring?



DOMAIN 4

TRANSITION MONITORING AND VISIBILITY

Are rigorous monitoring processes in place for: regimen change and patient outcomes, ARV stock levels, overall transition progress?



Findings

Findings of the Country Needs Assessment for South Africa are presented on the following pages by functional domain. Each functional domain is composed of multiple benchmarks. For each benchmark, the assessment specifies a “need rating” of low, moderate, or high along with a brief narrative justification summarizing the most relevant and compelling details behind that rating.

DOMAIN 1: ENABLING ENVIRONMENT (POLICY, ADVOCACY, AND FINANCE)

POLICY

BENCHMARK 1.1: Optimized ARVs are registered by the national drug regulatory authority (NDRA)

NEED RATING: MODERATE

Analyses of ARV commodity markets suggest that NDRA approval of an ARV product from 2+ suppliers is needed to ensure competitive pricing and stable supply. South Africa's next tender is expected in October 2017. In the past, new product introduction has been delayed by a lengthy and opaque Medicines Control Council (MCC) approvals process. An MCC backlog plan is now in place, and advocacy by Wits Reproductive Health and HIV Institute (WRHI), Clinton Health Access Initiative (CHAI), Treatment Action Campaign (TAC), and others is underway to promote the timely approval of DTG and TAF products, with top priority accorded to a DTG-containing FDC. Single-agent DTG has received approval from the MCC, and TAF is under consideration by the MCC expert committee. Registration of key formulations is expected to be completed in 12 months from March 2017, thanks to fast-tracking. A more autonomous NDRA (South African Health Products Regulatory Authority [SAHPRA]), which will not require National Department of Health (NDOH) approval for new products, is slated to replace MCC in April 2017. Support is needed to ensure that the registration of TLD and TAF is prioritized.

BENCHMARK 1.2: Optimized ARVs are included on essential medicines list and national treatment guidelines

NEED RATING: MODERATE

ARV products must be included in South Africa's Standard Treatment Guidelines (STG) and Essential Medicines List (EML) in order to be incorporated into a tender. Neither DTG nor TAF is included in South Africa's 2015 STG. However, the NDOH has a clear process for incorporating new ARV products into the STG with an estimated peer-review time frame of three to four months. This process can be triggered by changes to WHO guidelines, new drug registration, and/or release of local clinical/trial data. Support is needed to ensure that this process is initiated for TLD and TAF.

ADVOCACY

BENCHMARK 1.3: ART optimization is reflected in national care and treatment priorities

NEED RATING: LOW

South Africa's National Strategic Plan on HIV, TB, and Sexually Transmitted Infections 2017-2022 specifically cites preparations for optimized ARVs as part of its national rollout of universal test-and-treat, and the national government is actively considering the inclusion of optimized ARVs including TLD, TAF products, and injectable ARVs in the STG.

BENCHMARK 1.4: Providers and patients know the importance of optimized products and exhibit high demand for/uptake of same

NEED RATING: LOW

South Africa benefits from robust and influential civil society networks that actively promote and implement training and treatment education for providers and recipients of care. The CHAI-UNITAID Optimal ARV project will be funding activities to generate demand for TLD in South Africa once the regimen is formally adopted. UNITAID is also providing separate funding to WRHI, TAC, and Southern Africa HIV Clinicians Society (SAHCS) to increase treatment literacy among community and activist organizations and health care workers.

BENCHMARK 1.5: Optimized products have support from other stakeholders positioned to influence the pace and outcome of scale-up efforts

NEED RATING: MODERATE

In general, support for DTG is strong and widespread. Supplemental advocacy may be needed around around TAF as well as ART optimization in general, especially at the sub-national level. Some informants reported that instructions to provinces during past ARV transitions were not consistently accompanied by clear messages about the reasons for and benefits of the changes. UNITAID's planned funding to WRHI, TAC, and SAHCS includes policymakers as one of the target groups for demand generation.

DOMAIN 1: ENABLING ENVIRONMENT (POLICY, ADVOCACY, AND FINANCE), CONTINUED

FINANCE	<p>BENCHMARK 1.6: Optimized products are financially accessible to patients</p> <p>ARVs are provided free of charge to all patients receiving care in the public sector.</p>	NEED RATING: LOW
	<p>BENCHMARK 1.7: Sustainable funding source for scale-up of optimized products exists</p> <p>The South African Government funds 91 percent of national ARV purchases. Projections show that, at scale, South Africa will be able to procure TAFx_D for roughly half of what it currently pays for TLE, meaning that the country can double its ART enrollment with only a marginal impact on its drug budget. However, ARV procurement will remain costly and it is essential to ensure that public funding is continually allocated to RSA's HIV response.</p>	NEED RATING: MODERATE

<p>CRITICAL MILESTONES:</p> <ul style="list-style-type: none"> • MCC/SAHPRA approval and registration of DTG-containing FDCs and TAF products • Inclusion of DTG, TAF, in STG and EML 	<p>OVERALL NEED RATING:</p> <p style="background-color: #007bff; color: white; padding: 2px;">LOW</p> <p style="background-color: #6c757d; color: white; padding: 2px;">MODERATE</p>
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DOMAIN 2: PLANNING PROCESSES AND TOOLS

FORECASTING	<p>BENCHMARK 2.1: Accurate projections of market demand exist at national level NEED RATING: LOW</p> <p>NDOH and CHAI conduct national ARV demand forecasting that already incorporates some optimized ARV products and will be developing forecasts for the upcoming ARV tender using tested tools for scenario modeling and accurate demand projection.</p>
	<p>BENCHMARK 2.2: System in place to coordinate supply and demand at decentralized level NEED RATING: MODERATE</p> <p>ARV forecasting and supply management capacity and performance vary across provinces, as evidenced by variable provincial performance in management and mitigation of ARV stockouts.</p>
TENDERS AND PROCUREMENT	<p>BENCHMARK 2.3: Tenders are optimized for low cost and supply stability NEED RATING: LOW</p> <p>South Africa's ARV tendering and procurement methods include use of multiple suppliers and multi-year contracts to achieve the lowest prices in the world.</p>
	<p>BENCHMARK 2.4: Timing of tenders aligns to enable efficient uptake of optimized products NEED RATING: MODERATE</p> <p>Minimizing the time between the global debut of optimized ARVs and their introduction in South Africa may require changes to the timing of drug tenders. A national Tender Working Group has been formed to ensure alignment of the next tender with availability of TLD. The government is expected to release specifications of the upcoming tender in October 2017, review bids from December 2017 to January 2018, and award new contracts before April 2018. (A multi-month extension to the current tender is also possible in the event that TLD is not available from multiple suppliers by late 2017; continual monitoring is needed in order to ensure optimal timing between the tender and availability of new products).</p>
	<p>BENCHMARK 2.5: Optimized products are procured in sufficient quantity and quality to satisfy demand NEED RATING: MODERATE</p> <p>At present, it is unclear if the supply of optimized products (and the number of suppliers of each product) will be sufficient to meet demand and tender requirements in South Africa. Continual monitoring of the DCGI rule, which could potentially hinder supply of DTG- and TAF-containing products from Indian manufacturers, is needed.</p>
PLANNING AND TARGETS	<p>BENCHMARK 2.6: Plan for phased rollout of optimized products across geographies and sub-populations exists (with time-bound targets) NEED RATING: HIGH</p> <p>To date, no national product launch and scale-up plan has been developed for DTG (since there are outstanding questions about which combinations/formulations will be approved, recommended and rolled out), nor has a tentative schedule for developing this plan been set. Once TLD is adopted, it will be critical to develop both a national plan with time-delimited targets and province-specific plans and targets that support timely implementation.</p>
	<p>BENCHMARK 2.7: Roles and responsibilities of actors involved in scale-up are defined and agreed to NEED RATING: MODERATE</p> <p>Further refinement of roles and responsibilities with respect to new product introduction and subsequent scale-up will be needed to support a smooth transition in South Africa. The functions of central and decentralized government, advocacy groups, clinicians, and implementing partners, across key sectors will need to be concretely defined in conjunction with the development of the product launch and scale-up plan.</p>
<p>CRITICAL MILESTONES:</p> <ul style="list-style-type: none"> Align timing of 2018 tender to maximize uptake of DTG Develop phased transition plan complete with time-bound targets <p style="text-align: right;">OVERALL NEED RATING: MODERATE</p>	

DOMAIN 3: SERVICE DELIVERY CAPACITY

PROVIDER READINESS	<p>BENCHMARK 3.1: Providers are equipped with the knowledge and skills to effectively transition their ART patients to optimized products</p> <p>Because most providers were involved in previous ARV transitions (particularly the transition to 1L TLE FDC), providers' baseline knowledge of the transition process is fairly strong. To increase clinical knowledge of specific optimized combinations and formulations, SAHCS provides optimization-focused learning opportunities to its members (who include approximately 60 percent of all doctors in the country). However, additional training curricula and opportunities may be needed for other health care worker cadres involved in patient care, viral load (VL) monitoring, and drug management.</p>	NEED RATING: MODERATE
	<p>BENCHMARK 3.2: National standard operating procedures (SOPs), training materials, and job aids include clear messages about ART optimization and enhanced patient monitoring</p> <p>Revisions to clinical SOPs, training materials, and job aids to incorporate guidance on use of optimized ARV products and enhanced patient monitoring have not been initiated.</p>	NEED RATING: MODERATE

ARV DISTRIBUTION	<p>BENCHMARK 3.3: A functional supply chain links optimized products to all access points</p> <p>Supply forecasting and distribution challenges in provinces have caused repeated stockouts in South Africa, including ARV stockouts. While high-volume 1L regimens such as TLE have been less prone to stockouts than lower-volume ARVs (except in Eastern Cape), demonstrated supply chain weaknesses pose a potential threat to South Africa's ability to ensure that optimized 1L regimens reach all patients in all provinces in a timely manner. Some actions have been taken to improve supply stability for ARVs. For instance, the current tender requires that suppliers deliver ARV drugs directly to (or closer to) patient access points, rather than relying on health workers employed by the government to make deliveries. In addition, last-mile delivery innovations, such as ARV dispensing at private pharmacies and chronic dispensing units, have been introduced. However, continual monitoring is needed to ensure that that real-time facility-level uptake informs supply forecasts to avoid future stockout risks as optimized 1L regimens are introduced.</p>	NEED RATING: MODERATE
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<p>CRITICAL MILESTONES:</p> <ul style="list-style-type: none"> • Train and prepare health care workers to effectively implement transition to TLD, including through enhanced monitoring of patient outcomes and ARV stocks 	<p>OVERALL NEED RATING:</p> <p>MODERATE</p>
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DOMAIN 4: TRANSITION MONITORING AND VISIBILITY

PATIENT MONITORING	<p>BENCHMARK 4.1: Providers perform enhanced monitoring of patient outcomes (including VL suppression, retention, and adherence) during and after regimen change</p> <p>Baseline provider capacity in South Africa is comparatively strong, but intensified mentoring and supplemental chart reviews have proven to be critical factors in the success of past ARV transitions. Given the intensified focus on viral suppression under 90-90-90, South Africa will need to ensure that all providers are equipped to properly carry out enhanced patient monitoring during the transition period, as new and existing patients are initiated on optimized regimens.</p>	NEED RATING: MODERATE
	<p>BENCHMARK 4.2: De-identified patient outcomes data from Electronic Medical Record/Electronic Patient Tracking System (EMR/ePTS) are aggregated to enable tracking of sub-national and national performance</p> <p>South Africa's national EMR utilizes unique identifiers but has only been rolled out at a limited number of sites. Use of the national HIV EMR system (Tier.net) to track patient linkages remains sub-optimal. In order to track both patient outcomes and aggregate transition progress effectively, these systems require strengthening and expansion, as well as a functional link to lab results data from the National Health Laboratory Service.</p>	NEED RATING: MODERATE
STOCK MONITORING	<p>BENCHMARK 4.3: Stocks of optimized products within RSA are actively monitored in a transparent manner</p> <p>The Stop Stockouts campaign (led by TAC, SAHCS, Médecins Sans Frontières [MSF], Rural Doctors Association of Southern Africa [RuDASA], and Section 27) enables immediate reporting of ARV stockouts by any observer or affected individual via a hotline, systematically communicates these reports to NDOH, and holds provincial authorities accountable for resolving reported stock issues. Ensuring that Stop Stockouts has the resources and capacity to continue this important work during the upcoming ARV transition is of high importance.</p>	NEED RATING: MODERATE
M&E	<p>BENCHMARK 4.4: Monitoring and evaluation (M&E) plan and process for product launch and scale-up defined</p> <p>As no national product launch and scale-up plan has been developed, a M&E plan and process have yet to be defined. This is an important benchmark, particularly given gaps and weaknesses in the national medical record system (described under 4.2).</p>	NEED RATING: HIGH
<p>CRITICAL MILESTONES:</p> <ul style="list-style-type: none"> Define M&E plan and process to accompany national product launch and scale-up plan 		<p>OVERALL NEED RATING:</p> <p>MODERATE</p>

Summary of Findings

South Africa has strong human and institutional capacity in several domains that underpin the ART optimization process. By allocating resources and energy to target areas with the greatest need and potential impact, the Government of South Africa and its partners can accelerate the introduction of DTG-based FDCs, TAF, and other optimized ARV products and their scale-up to all people living with HIV.



DOMAIN 1

ENABLING ENVIRONMENT

The proven reach and effectiveness of South Africa's civil society networks in the areas of demand generation, treatment literacy, and stockout reporting and accountability, in combination with forthcoming funding from UNITAID for demand generation, suggests that advocacy is an area of relatively low need (though it is important to ensure that activities proceed as planned, especially at the sub-national level). Having established the largest ART program in the world, South Africa already achieves consistently low ARV prices through economies of scale; as a matter of policy, South Africa also provides ARVs to all public-sector patients free of charge, making them accessible to all people living with HIV. The areas of greatest need with respect to creating an enabling environment for ART optimization in South Africa are 1) obtaining NDRA approval for DTG-containing FDCs and 2) incorporating these products into the Standard Treatment Guidelines and Essential Medicines List in time to ensure they can be included in the upcoming tender.



DOMAIN 3

SERVICE DELIVERY CAPACITY

Though each province faces its own challenges with respect to ART service delivery and ARV distribution and logistics, providers and pharmacists are generally well acquainted with the programmatic and clinical requirements of ARV transitions. Recent innovations with respect to last-mile distribution of ARVs promise to facilitate access for patients in areas that have experienced habitual ARV stock-outs. The areas of greatest need with respect to service delivery capacity include 1) ensuring that providers and pharmacists understand the benefits of optimized regimens and their role(s) in scaling them up; and 2) clearly delineating responsibility for transitioning patients and transporting ARV drugs from provincial depots to final access points.



DOMAIN 2

PLANNING PROCESSES AND TOOLS

South Africa employs good practices for national forecasting and tendering – including multi-year tenders and split tendering – in order to maximize cost savings and protect against supply instability. At the sub-national level, forecasting and quantification performance varies across provinces and requires reinforcement to ensure adequate ARV supply throughout the transition period. The area of greatest need with respect to planning processes and tools is developing a phased national rollout plan for the optimized first-line regimen, complete with sub-national targets, defined roles and responsibilities, and demand generation and other preparatory activities.

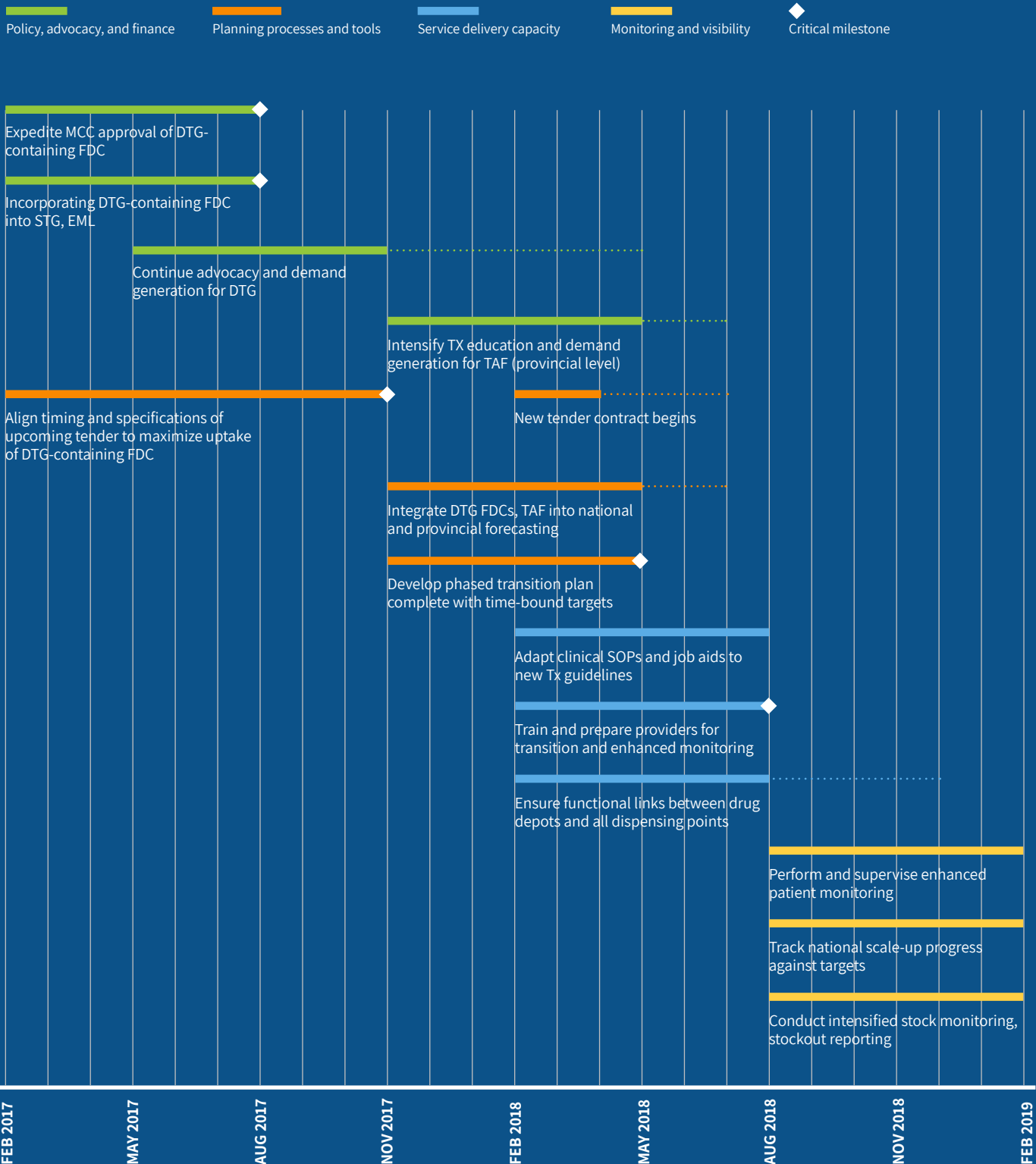


DOMAIN 4

TRANSITION MONITORING AND VISIBILITY

The Stop Stockouts partnership performs a valuable service by ensuring timely reporting of and accountability for drug stock-outs; this function will be essential during the upcoming first-line transition. In the area of patient outcomes and transition monitoring, electronic patient-level and aggregate databases for ART exist, but they are not fully harmonized or integrated. The area of greatest need with respect to transition monitoring and visibility is the development and implementation of a comprehensive M&E plan to accompany the national rollout plan. The M&E plan should include expected timetables and formats for reporting on regimen changes, stock levels and other critical transition parameters at the facility, sub-district, district, and provincial levels, in order to facilitate periodic “snapshots” of national transition progress.

ILLUSTRATIVE PRODUCT INTRODUCTION WORK PLAN: SOUTH AFRICA³



3. The dates outlined in this Illustrative Work Plan are only relevant in the case that the October 2017 tender release timeline is not extended.

Analysis of South Africa's capacity and readiness in key areas pertaining to the introduction of new ARV products suggests a critical path that hinges heavily on policy milestones, as well as operational planning and preparation. As conveyed in the illustrative work plan on page 12⁴, in order to prepare for a national launch of a DTG-containing first-line regimen in mid-2018, should the current tender not be extended, South Africa must:

- Secure MCC approval of DTG FDCs from multiple suppliers (target date: August 2017)
- Incorporate DTG-based FDCs into the Standard Treatment Guidelines and Essential Medicines List (target date: August 2017)
- Include DTG FDCs in the upcoming tender (target date: October 2017)
- Align timing of upcoming tender to ensure access to optimized products from multiple suppliers (target date: October 2017)
- Develop a phased transition plan for product launch and scale-up, with sub-national targets and M&E plan (target date: March 2018)
- Train and prepare providers, pharmacists, and managers for transition responsibilities, including enhanced monitoring (target date: July 2018)

If these critical milestones are met, and planned demand generation and treatment literacy campaigns proceed as expected, South Africa should be among the first countries in the world to realize the full health and financial benefits of adopting optimized ART.

In collaboration with WRHI, CHAI, and other partners, the Government of South Africa has made tremendous progress towards several of the milestones listed above. Additional technical assistance for national and sub-national planning, implementation, and monitoring related to the introduction of optimized ARVs is available to the Government of South Africa through founding **OPTIMIZE** and **OPTIMAL** consortium partners, including WRHI, ICAP at Columbia University, TAC, Southern African HIV Clinicians Society, and CHAI.

Specific tasks and functions for which the South African Government may request technical assistance from **OPTIMIZE** include:

- Definition of stakeholder roles (NDOH, PDOH, care providers, pharmacists, PEPFAR implementing partners, civil society organizations) with respect to new product introduction and scale-up;
- Target-setting and operational planning for introduction and scale-up of one or more optimized products;
- Design and implementation of early adopter research on uptake and outcomes of optimized products;
- Support for enhanced patient monitoring during the transition to optimized ART regimens; and
- Other national priorities with respect to optimization, as appropriate and feasible.

4. As in the Illustrative Work Plan on page 12, the dates outlined in this section are only relevant in the case that the October 2017 tender release timeline is not extended.

IF THESE CRITICAL MILESTONES ARE MET SOUTH AFRICA SHOULD BE AMONG THE FIRST COUNTRIES IN THE WORLD TO REALIZE THE FULL HEALTH AND FINANCIAL BENEFITS OF ADOPTING OPTIMIZED ART.



Annex

APPENDIX 1: LIST OF INTERVIEWEES

	Date	Name	Title	Organization
Clinical	13 Sep 2016	Francois Venter	Deputy Executive Director	Wits RHI
Policy	12 Sep 2016	Celicia Serenata	Technical Lead	Wits RHI
Clinical	13 Sep 2016	Mohammed Majam	Programme Manager	Wits RHI
Clinical	13 Sep 2016	Michelle Moorhouse	Senior Clinician	Wits RHI
Clinical	21 Sep 2016	GP Akpomiemie	Trial Operations Coordinator	Wits RHI
Impl, Procur	22 Sep 2016	Bada Pharasi	Country Project Director, Systems for Improved Access to Pharmaceuticals & Services	Management Sciences for Health (MSH)
Procur	22 Sep 2016	Jorge Quevedo	Acting Country Director	CHAI
Advocacy	15 Sep 2016	Lauren Jankelowitz	CEO	Southern African HIV Clinicians Society
Advocacy	14 Sep 2016	Marcus Low	(formerly) Head of Policy	(formerly) TAC
Policy	16 Sep 2016	Yogan Pillay	Deputy Director-General: HIV, TB and Maternal and Child Health	Department of Health
Policy	23 Sep 2016	Nono Simelela	Social Policy Advisor to the Deputy President of South Africa	Office of the President
Policy	20 Sep 2016	Fareed Abdullah	CEO	South African National AIDS Council (SANAC)
Imp	21 Sep 2016	Sandile Buthelezi	Country Director	ICAP
Imp	16 Sep 2016	Steve Smith	Health Attaché	US Embassy
Imp	16 Sep 2016	Charles Pill	PEPFAR Country Coordinator	US Embassy
Imp	16 Sep 2016	Paul Mahanna	Deputy Director, Health Office	USAID
Imp	20 Sep 2016	Raymond Chimatira	Adult Treatment Specialist	CDC
Imp	20 Sep 2016	Thomas Heller	Branch Chief, Care and Treatment Branch, Division of Global HIV/AIDS & TB	CDC
Policy (regulatory)	31 May 2016	Christine White	Regulatory Affairs Manager	Mylan
Policy	19 Sep 2016	Helen Schneider	Professor and Director	University of the Western Cape
Policy	19 Sep 2016	Andy Gray	Senior Lecturer	University of KwaZulu-Natal
		Andrew Boule*	Associate Professor	University of Cape Town
		Gavin Steel*	Chief Director, Sector Wide Procurement	Department of Health
		Zukiswa Pinini*	Senior Medical Manager	Department of Health
		Rehmeth Fakroodeen*	HSS Team Lead	CDC

*Individuals were contacted but either did not respond or did not have availability.

APPENDIX 2: INTERVIEW GUIDE

Topics for discussion

Interviewees will be asked relevant questions according to their area of expertise. Interviews will be structured around the following core areas (shown below with corresponding example questions):

OVERALL:

In a recent global stakeholder assessment conducted by ICAP⁵, the following country-level programmatic gaps were identified across multiple countries. Do you foresee any of these as barriers to introduction and scale-up of potential new optimized ARVs in South Africa? Why or why not? What are potential interventions to reduce these barriers?

- NDRA staffing shortages and inadequate dossier management systems
- Fragmented or inadequate planning and operational guidance for ARV transitions
- Reluctance among procurement agents to order new ARV products from suppliers that have resolved past fulfillment challenges
- Limited awareness of optimal ARV drug availability and benefits among recipients and health care providers
- Poor visibility of ARV drug stocks leading to facility-level stock-outs

What are additional barriers to introduction and scale-up of the potential new optimized ARVs in South Africa? What approaches could be taken to reduce these barriers?

POLICY, FINANCING, AND ADVOCACY:

- With the current tender commitments through March 2018, is there flexibility to adjust the next tender process to include new ARVs if data becomes available off-cycle?
- What is the process and timing for product inclusion on the Essential Medicines List? What data or evidence is recommended or required?
- What is the process and timing for product inclusion in the standard treatment guidelines? What data or evidence is recommended or required? How will the process be influenced by whether or not the drugs are included in the WHO Guidelines?
- What advocacy would be needed with clinicians, patients, and other groups? Who is best placed to implement this? What lessons are there from past advocacy efforts to build on (e.g. when shifting to FDCs in South Africa)?

CLINICAL EVIDENCE AND REGULATORY:

- When is the transition from SAHPRA to MCC? What are expected changes to the regulatory process and timing post-transition?
- What additional clinical evidence would be needed to expedite the approval process or expand the new product's approved uses? Is it anticipated that current and recent studies will generate sufficient evidence for relevant populations (including pregnant women, TB co-infected, and children)?
- Are there any potential challenges with obtaining timely results from the clinical studies based in South Africa (such as patient enrollment, drug supply from manufacturers, etc.)?

MANUFACTURING AND DISTRIBUTION:

- What balance of local and global manufacturing will ensure consistent supply of the product(s)? How will the Indian government (DCGI) regulations requiring local clinical trials for any generics manufactured and licensed in India impact drug availability and timing in South Africa?
- Are production economics favorable?
- What is the process and timing for adding new ARV drugs to the procurement and distribution systems?
- What is the country status of offering HIV treatment to all people living with HIV? Will current procurement and distribution systems be able to handle the increased volume?
- Are there any anticipated challenges with current and future visibility of facility stock levels and regular delivery to all users? What is the status of non-facility based distribution mechanisms?

MARKET AND USER:

- What awareness/demand generation/education activities would be needed for the introduction of new ARV drugs? Are any such activities currently ongoing and/or planned?
- Is any user-preference research currently ongoing and/or planned (such as pack size preference, harmonized formulation identifiers, etc.)?
- What would be the advantages and/or disadvantages of pooled procurement with the Southern African Development Community (SADC)?

COORDINATION:

- Based on previous ARV transitions, what is the best plan for transition (by whom, how, steps and timeline)? Who are the most important stakeholders and collaborators?
- Are there particular planning tools that will be used for the transition?
- What questions do you have for other stakeholders?

5. The purpose of the assessment was to map out key stakeholders' existing and planned activities with respect to the introduction of optimized ARV products, to document select best practices and tools relevant to those activities, and to identify programmatic gaps and areas for action with a view to streamlining and expediting ARV optimization in LMICs over the next five years.



The **OPTIMIZE** project is a global consortium dedicated to rapidly improving treatment outcomes for people living with HIV by optimizing ARV drugs and formulations and accelerating their introduction in low- and middle-income countries. Founding members of the **OPTIMIZE** consortium include five leading private and public sector organizations: (1) Wits Reproductive Health and HIV Institute (Wits RHI), an established PEPFAR implementing partner with expertise in research, program implementation, policy, and training; (2) ICAP at Columbia University (ICAP), one of the largest PEPFAR implementing partners, with extensive experience providing site, regional, and national support in the scale-up of HIV services and conducting studies on HIV adherence and retention; (3) Mylan Laboratories Limited (Mylan), a global generic and specialty pharmaceuticals company with drug development and manufacturing capacity to achieve lower yet sustainable pricing; (4) the University of Liverpool (UoL), a leading academic research institution with unique capabilities in Solid Drug Nanoparticle (SDN) technology; and (5) the Medicines Patent Pool (MPP), a United Nations-backed not-for-profit organization with a public health driven approach to lowering HIV medicine prices through voluntary licensing and patent pooling. For further information or to request technical assistance from **OPTIMIZE**, please contact Nandita Sugandhi, ICAP Product Introduction Coordinator, at nss14@cumc.columbia.edu or +1(212) 305-7085.



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