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Kenya Situational Analysis

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Executive Summary





Over the past decade, Kenya has established itself as a regional leader in antiretroviral therapy (ART) optimization including successfully engineering two major first-line transitions to date. However, the process of introducing optimal antiretrovirals (ARVs) can be challenging and to avoid potential issues, country programs, such as Kenya's, require a foundational understanding of their readiness in four key domains related to new product introduction. The OPTIMIZE Kenya Situational Analysis focuses on the following domains: 1) Policy, Advocacy, and Finance; 2) Planning Processes and Tools; 3) Service Delivery Capacity; and 4) Transition Monitoring and Visibility, each of which is divided into a number of sub-domains. Drawing on quantitative and qualitative data, the Situational Analysis assigns a need rating of low, moderate, or high to each sub-domain and identifies priority areas to address to ensure that upcoming transitions to optimized products maximize health and budgetary benefits.

Overall, the Kenya program is quite strong, and ratings across the domains and sub-domains indicated low levels of need. A summary of the findings from the Analysis is below:

ABBREVIATIONS

3TC	Lamivudine	GoK	Government of Kenya	PPB	Pharmacy and Poisons Board
ADR	Adverse drug reactions	HIV	Human immunodeficiency virus	PSM	Procurement and Supply Management Project
ADT	ARV dispensing tool	IP	Implementing Partner	PV	Pharmacovigilance
AE	Adverse event	IRIS	Immune Reconstitution Inflammatory Syndrome	PWID	People who inject drugs
AfroCAB	African Community Advisory Board	JOOTRH	Jaramogi Oginga Odinga Teaching and Referral Hospital	TAF	Tenofovir alafenamide fumarate
AIDS	Acquired immune deficiency syndrome	KEMSA	Kenyan Medical Supplies Authority	TDF	Tenofovir disoproxil fumarate
ART	Antiretroviral therapy	LIS	Laboratory Information System	TLD	Tenofovir/Lamivudine/Dolutegravir
ARV	Antiretroviral	LMIC	Low- and middle-income countries	TLE	Tenofovir/Lamivudine/Efavirenz
ATV/r	Atazanavir/ritonavir	MOH	Ministry of Health	TWG	Technical Working Group
CDC	Centers for Disease Control	MSF	Médecins Sans Frontières	UNAIDS	Joint United Nations Programme on HIV/AIDS
CHAI	Clinton Health Access Initiative	NASCOP	National AIDS and STI Control Programme	USAID	U.S. Agency for International Development
CRP	WHO Collaborative Registration Process	NEPHAK	Network of People Living with HIV/AIDS in Kenya	USFDA	U.S. Food and Drug Administration
CSC	Commodity Security Committee	NNRTI	Non-nucleoside reverse transcriptase inhibitor	VL	Viral load
d4T	Stavudine	NVP	Nevirapine	WHO	World Health Organization
DTG	Dolutegravir	PEPFAR	President's Emergency Plan for AIDS Relief	ZDV	Zidovudine
EDS	Enhanced Data System	PLHIV	People living with HIV	ZLN	Zidovudine/Lamivudine/Nevirapine
EFV	Efavirenz				
EMR	Electronic medical record				
FDC	Fixed-dose combination				
GMP	Good manufacturing practices				

Table 1: Summary of key points from analysis by domain

 <p>DOMAIN: Policy, Advocacy and Finance</p> <p>HIGHLIGHTS: There is widespread support for and appreciation of the need for optimization among stakeholders and a recognized need to simplify the number of regimens in use.</p> <p>The Kenyan Medical Supplies Authority (KEMSA) has a record of achieving competitive pricing for ARV products with minimal supply interruptions due to volume discounts and a strong strategy for maximizing resources of the three major ARV buyers.</p> <p>There is an organized and transparent drug procurement process.</p>	<p>OVERALL RATING: LOW</p>
 <p>DOMAIN: Planning Processes and Tools</p> <p>HIGHLIGHTS: Kenya has a national ARV supply plan and routine data flows in a timely and efficient manner from ART facilities to the National AIDS and STI Control Programme (NASCOP) and KEMSA.</p> <p>Though there is limited visibility into last-mile distribution and consumption data from lower-level facilities, KEMSA and NASCOP have a strong reputation for on-time distribution and commodity security.</p>	<p>OVERALL RATING: LOW</p>
 <p>DOMAIN: Service Delivery Capacity</p> <p>HIGHLIGHTS: The Ministry of Health (MOH) /NASCOP provides clear guidance to healthcare providers and health management teams through circulars that are widely disseminated.</p> <p>Providers consistently demonstrate strong capacity with respect to ART, but those at lower-level facilities will likely require additional on-site mentorship and training to ensure the commended transition is smooth.</p>	<p>OVERALL RATING: LOW</p>
 <p>DOMAIN: Transition Monitoring and Visibility</p> <p>HIGHLIGHTS: A system for reporting adverse drug reactions (ADR) exists, but reporting rates are low and vary across geographic areas. The pharmacovigilance training module has been updated to address this. Training on pharmacovigilance is included in health workers training in ART Optimization sensitization package.</p> <p>The Commodity Security Committee (CSC) is able to monitor overall ARV stocks and consumption data at ARV ordering sites, but not at the satellite sites.</p>	<p>OVERALL RATING: MODERATE</p>

In response to the findings outlined in Table 1, it is recommended that Kenya implement the following actions:

1. Streamline and simplify guidance on preferred first, second and third-line ART regimens.
2. Utilize multiple communication channels to ensure that healthcare workers at all levels, including those at lower-level facilities, are reached with transition information and guidance on use of optimized ART.
3. NASCOP should strengthen pharmacovigilance. Suggested actions include 1) strengthening PV systems for assessing ADRs in patients transitioning to optimized ARVs; 2) increase uptake and use of the pharmacovigilance (PV) system through dedicated training and on-site mentorship; and 3) seek direct input from and collaborate with other MOH programs so that system enhancements benefit all end users of PV data.

Purpose

OPTIMIZE, a project supported by the U.S. Agency for International Development (USAID) through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), aims to accelerate the development, testing and market introduction of optimized ARV products to support the best possible treatment outcomes for people living with HIV (PLHIV) 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 tuberculosis (TB) patients), and 2) adapted to resource- and infrastructure-constrained environments (i.e. affordable, heat-stable and available in fixed-dose combinations [FDC]). Optimized ARVs are well tolerated, have lower toxicity and higher genetic barrier to resistance, which reduces the risk of treatment failure by supporting patient adherence and inhibiting the development of drug resistance. The resulting increase in rates of viral suppression offers significant health benefits at individual and population levels by both limiting disease progression and decreasing rates of HIV transmission.

The antiretroviral therapy (ART) 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 low- and middle-income countries (LMIC) efficiently

and effectively. At the program level, issues such as national policy and regulatory barriers, tendering and procurement challenges, supply chain interruptions, slow uptake by prescribers, and patient apprehension have hindered some past transitions to new ARV products. To avoid these and other stumbling blocks during the transition to optimized ARV products such as dolutegravir (DTG) and tenofovir alafenamide fumarate (TAF) in the next two to three years, countries require a foundational understanding of their readiness in key domains relating to new product introduction.

The OPTIMIZE Kenya Situation Analysis 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, each of which is divided into a number of sub-domains. Drawing on quantitative and qualitative data, the Analysis assigns a need rating of low, moderate, or high to each sub-domain and identifies priority bottlenecks or weaknesses where action is required to ensure that upcoming transitions to optimized products maximize health and budgetary benefits. In Kenya, the Situation Analysis accorded special attention to pharmacovigilance (PV) systems, as PV is a current priority for the Ministry of Health (MOH) and other national stakeholders.



Country Context

Kenya faces a generalized human immunodeficiency virus (HIV) epidemic with an adult prevalence of 5.9%ⁱ and is logging rapid gains towards the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets (90% of people living with HIV (PLHIV) know their HIV status, 90% of people diagnosed with HIV are on antiretroviral therapy (ART), and 90% of ART patients are virally suppressed). As of March 2017, approximately 72% of the estimated 1.5 million PLHIV in Kenya knew their status, while 88% of diagnosed PLHIV were receiving ART.ⁱⁱ According to the NASCOP Viral Load dashboard, 85% of viral load tests administered to adult ART patients in 2017 indicated viral suppression; however, this rate was only 65% among pediatric ART patients under the age of 15.ⁱⁱⁱ The lack of acceptable, easy-to-administer ARV formulations for very young children, as well as the lower barrier to resistance of non-nucleoside reverse transcriptase inhibitors (NNRTI) drugs found in >75% of pediatric first-line regimens,^{iv} are two factors contributing to lower rates of adherence and viral suppression among children.^v

Over the past decade, Kenya has established itself as a regional leader in ART optimization. It was among the first LMICs to implement a focused phase-out of stavudine (d4T)^{vi}, and the Government of Kenya's (GoK's) 2016 commitment to adopt DTG-based regimens into its treatment guidelines was instrumental in negotiating an affordable launch price for DTG 50mg single tablets.^{vii}

The complete phase-out of d4T in Kenya was successful, though protracted. In contrast, the phase-in of the fixed-dose combination (FDC) tablet of tenofovir disoproxil fumarate (TDF) 300mg + lamivudine (3TC) 300mg + efavirenz (EFV) 600mg (TLE600) has, to date, been a slow and incomplete process, because patients were transitioned from d4T to multiple replacement regimens. Today, significant first-line complexity persists; as of mid-2016, only 59% of Kenya's 940,000 adult first-line patients were on TLE600.

Figures 1 and 2 (page 6) show the distribution of key first-line and second-line regimens among adults and adolescents in Kenya as of July 2017.^{viii}



i. Kenya HIV Estimates, 2015.

ii. PEPFAR Kenya COP SDS 2017. P. 32.

iii. NASCOP Viral Load Dashboard, Age Category Breakdown for Viral Load Suppression. Accessed December 11, 2017: <https://viralload.nascop.org>.

iv. NASCOP ART regimen splits for August 2017.

v. Interviewees noted that lack of an acceptable ART option for very young children has, in some cases, discouraged providers from prescribing ART.

vi. Phasing Out Stavudine: Progress and Challenges. Supplement to 2013 WHO Consolidated Guidelines. Available: http://www.who.int/hiv/pub/guidelines/arv2013/arv2013supplement_to_chapter09.pdf

vii. Three New Agreements Announced with the Potential to Expand Access to Innovative HIV Treatment in Low- and Middle-Income Countries (Joint CHAI/UNITAID/UNAIDS Press release). November 30, 2015. Available: http://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2015/november/20151130_PR_CHAI_UNITAID

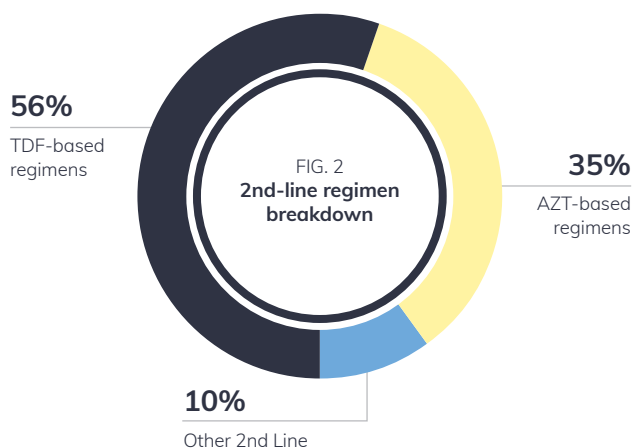
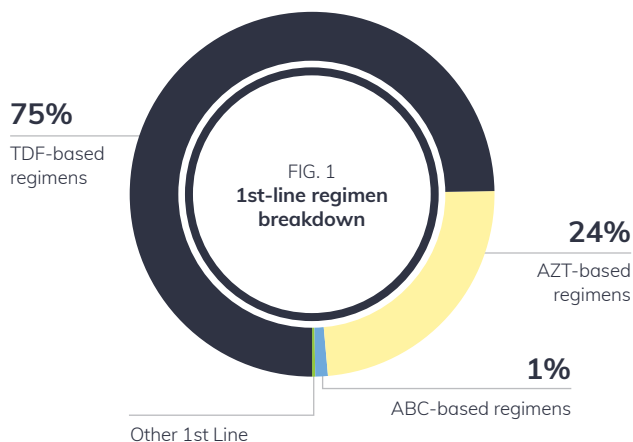
viii. National ART Program Stock Status Report (PowerPoint presentation). July 2017. Prepared for the Commodity Security Committee.

In July 2016, Kenya's MOH issued revised national treatment guidelines incorporating recommendations from the 2015 WHO Consolidated Guidelines on the use of antiretroviral drugs and for treatment and preventing HIV infection, including Test and Treat and differentiated care based on disease progression.^{ix} The guidelines maintain TLE600 as the preferred first-line treatment for adults while making provision for the future introduction of DTG-based regimens as an alternative option.^x In June 2017, the MoH disseminated a circular to all 47 counties and health facilities providing ART with recommendations for the introduction of DTG-containing regimens using DTG 50mg tablets for three patient populations: 1) current ART patients exhibiting EFV intolerance; 2) people who inject drugs (PWID), including those initiating or continuing ART; and 3) patients requiring or currently receiving third-line ART. Concurrently, select pilot sites have begun substituting DTG singles in place of NVP single tablets for adult patients taking TDF 300mg + 3TC 300mg + NVP 200mg, until an FDC of TDF+ 3TC+ DTG (TLD) becomes available. Once an FDC of TLD is available in Kenya,^{xi} the MoH expects to issue a Rapid Advice guidance document containing broad technical and operational guidance on ARV optimization including the phased introduction of the TLD FDC in adult first-line treatment (specific eligibility criteria and transition phasing parameters were still being formulated by NASCOP at the time of this assessment).

Note on TLE400: The formulation of an FDC with TDF, 3TC and a reduced dose of EFV, known as TLE400, is briefly mentioned in the 2016 national treatment guidelines though not listed as a preferred or alternative adult first-line regimen. The national program procured 600,000 packs of TLE400, which arrived in April 2017; however, there are no plans to order additional packs of the product or to further scale-up its use. NASCOP, in collaboration with stakeholders, has agreed on a plan to exhaust existing stocks of TLE400 at health facilities in Nairobi County.

Special Considerations: Kenya

- Low ART coverage and viral suppression among children and adolescents on ART
- Relatively complex distribution of first-line and second-line ARV regimens currently in use in adults and adolescents
- Weak pharmacovigilance system with limited reporting of ADR
- Need for close ARV pipeline monitoring and management to avoid wastage of ARVs
- Prior ART transition experience to guide a structured phase-in approach of new ARVs



ix. Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya: 2016 edition. Available: https://www.kma.co.ke/images/HIV_Dosage/ARV_guidelines_2016.pdf

x. Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya: 2016 edition. p92 (footnote). https://www.kma.co.ke/images/HIV_Dosage/ARV_guidelines_2016.pdf

xi. At present, the first shipment of generic TLD FDC is expected to arrive in Kenya in November - December of 2017.

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 the OPTIMIZE stakeholder landscape analysis. Consultations for this assessment were completed in September 2017.



DOMAIN 1

ENABLING ENVIRONMENT (POLICY, ADVOCACY, AND FINANCE)

To what extent are national policies, advocacy platforms, and financial processes ready to promote and facilitate new product introduction?



DOMAIN 2

OPERATIONAL PLANNING AND PREPARATION

To what extent do tools and processes for forecasting, tendering, target-setting, and transition monitoring require updating or adaptation?



DOMAIN 3

SERVICE DELIVERY SUPPORT

To what extent are ART service delivery models and healthcare workers prepared to introduce new ARV products and enhanced patient monitoring?



DOMAIN 4

TRANSITION MONITORING AND VISIBILITY

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



I. Enabling Environment (Advocacy, finance and policy)

Table 2: Enabling environment (Advocacy, finance and policy)

<p>BENCHMARK: Shared understanding of benefits of optimization</p> <p>JUSTIFICATION: Multiple stakeholder groups possess a strong understanding of and appreciation for optimization. Information about the side effects and other attributes of ARV drugs travels quickly.</p>	<p>NEED RATING: LOW</p>
<p>BENCHMARK: Political will and popular support for optimization</p> <p>JUSTIFICATION: There is widespread support for optimization, particularly if it will lead to sustainable cost savings and fewer or less severe side effects for patients.</p>	<p>NEED RATING: LOW</p>
<p>BENCHMARK: Financial requirements and resources</p> <p>JUSTIFICATION: There is no ARV funding gap for the current year, and Kenya has a track record of negotiating some of the lowest global prices for ARV drugs. However, Kenya currently relies on donor financing for 92% of its ARV needs.</p>	<p>NEED RATING: MODERATE</p>
<p>BENCHMARK: Transparent, streamlined drug registration (or waiver) process in place</p> <p>JUSTIFICATION: PPB has an organized and transparent drug registration process that includes an informal fast-track mechanism for drugs whose rapid approval is deemed to be in the public interest.</p>	<p>NEED RATING: LOW</p>
<p>BENCHMARK: Policy readiness (National Care and Treatment Guidelines)</p> <p>JUSTIFICATION: Guidelines include Treat All, Routine Viral Load Monitoring, and Differentiated Service Delivery models and make provision for the introduction of DTG-based regimens and other optimized products via issuance of a Rapid Advice Statement. Planned revision and launch of national ART guidelines by mid-2018.</p>	<p>NEED RATING: LOW</p>

Shared understanding of optimization benefits:

Knowledge of ARV optimization in general, and of the benefits of specific optimized drugs, is strong among national-level stakeholders. With respect to the value proposition for DTG in first-line treatment, program managers emphasized the increased importance of minimizing ARV-related ADR, especially now that Kenya's Test and Treat policy has extended ART to more asymptomatic patients, who may be less tolerant of treatment-related side effects. Stakeholders also noted DTG's ability to rapidly suppress viral load as an important characteristic, particularly in pregnant women who are diagnosed in their third trimester, (though at the time of this assessment, Kenya has not yet endorsed the use of DTG during pregnancy).

The National Empowerment Network of People Living with HIV/AIDS in Kenya (NEPHAK) partners with African Community Advisory Board (AfroCAB) and Unitaid to stay abreast of the latest evidence on ARV drugs and educate its member associations about this evidence. NEPHAK leadership acknowledged that PLHIV knowledge about the benefits of specific ARV products and formulations remains uneven and is weaker in rural areas compared to urban areas.

Political will and popular support for optimization:

Stakeholders agree on the importance of introducing optimized ARV products from both clinical and cost perspectives. However, while some stakeholders expressed a readiness to adopt TLD as a universal first-line regimen once an FDC becomes available, others preferred to see the regimen applied in a more targeted manner for patients with EFV intolerance and pregnant women who must achieve viral suppression quickly to minimize the risk of vertical transmission. There was pronounced debate on this question during the deliberative process of the 2016 guideline revision. While early concerns about the cost of TLD vis-à-vis TLE600 have since been alleviated following the announcement of a ceiling price agreement pricing TLD at a comparable price of \$75 per patient per year (PPPY), other concerns remain, such as the need to preserve the longevity of TLE600 (a safe, effective, tolerable regimen that can be used across all major patient populations). Some stakeholders expressed concern about exhausting DTG, the "most powerful regimen available," in first-line therapy, instead of reserving it for use in second-line regimens. NASCOP has also not yet reached consensus about which ARV regimen will be used as a second-line for patients experiencing treatment failure on DTG-containing regimens. However, discussions are currently ongoing in country to forge consensus on sequencing of optimized ARV regimens.

Financial requirements and resources:

The KEMSA has a record of achieving competitive pricing for ARV products with minimal supply interruptions due to volume discounts and a well-defined approach for maximizing the resources of the three major ARV buyers: the Global Fund, the President's Emergency Plan for AIDS Relief (PEPFAR), and the GoK. In 2016, Kenya's national budget for ARV drugs was just under \$160M, with Global Fund purchasing 50% of ARVs, PEPFAR purchasing 41% and GoK purchasing 9%. NEPHAK indicated that advocating for additional national resources for ARV drugs is a priority, while select other stakeholders expressed confidence that even in the face of potential reductions in external funding, the GoK would be able to mobilize additional resources to meet national treatment needs. An increase in domestic funding would need to come from an increased allocation within the GoK general budget, which is the source of funding for all health services, including HIV services.

KEMSA has a record of achieving competitive pricing for ARV products with minimal supply interruptions due to volume discounts and a well-defined approach for maximizing the resources of the three major ARV buyers.

Transparent, streamlined drug registration process:

The Pharmacy and Poisons Board (PPB) is responsible for assessing the quality, safety and efficacy of new pharmaceutical products submitted for local registration by drug manufacturers and determining whether or not to license new products. Three elements are required for the registration of a new ARV product: pre-registration laboratory analysis of product samples, verification of good manufacturing practices (GMP), and evaluation of technical data. Currently, PPB observes no exception to the first two requirements irrespective of whether a product's registration is routed through the WHO Collaborative Registration Procedure (CRP) or is the subject of a Public Interest request from the MoH. Thus, one major component of the CRP's value proposition to participating countries — that it reduces time to registration — is not applicable to Kenya under current PPB policies.

There is no formal "fast track" mechanism for registration of new drugs in Kenya, though the PPB is currently developing rules and parameters for such a mechanism. Standard time to registration for new drug applications is 18 months, consisting of 12 months for PPB review and six months for queries and responses between PPB and the applicant. However, the time for new pharmaceutical products to be registered is often shorter in cases where PPB receives a Public Interest request from MOH (generally issued when a drug has been pre-qualified by WHO and is considered a priority by MOH program leadership). In these cases, PPB will prioritize a product and/or allow for its import and distribution while full technical evaluation is underway; however, there is a strict requirement that all drugs — including those subject to a Public Interest request — go through GMP verification and pre-registration analysis before they are authorized for distribution.

Another factor that facilitates efficient new product introduction in Kenya is supplier behavior; most ARV suppliers now submit applications to the PPB at or around the time they submit applications to WHO and the United States Food and Drug Administration (USFDA), enabling PPB and stringent regulatory authority reviews to proceed concurrently. For instance, PPB has already approved the TLD FDC application submitted in 2016 by Aurobindo and is currently reviewing a TLD FDC application from Mylan. Both applications are being handled through the standard registration channel, and no registration-related delays are anticipated.

PPB is currently transitioning to a fully virtual process using an online drug registration portal that will allow applicants to upload forms and supporting materials in electronic format and make payments online. This innovation should streamline and expedite the drug registration process in the future once the transition is complete.

PPB is currently transitioning to a fully virtual process using an online drug registration portal that will allow applicants to upload forms and supporting materials in electronic format and make payments online. This innovation should streamline and expedite the drug registration process.

Policy readiness:

Before a new ARV product can be introduced or prescribed in Kenya, it must be formally integrated into the national treatment guidelines. The latest iteration of the guidelines, published in July 2016, introduces several important changes. These include the following recommendations: treat all individuals with confirmed HIV diagnosis, irrespective of WHO clinical stage or CD4 count; differentiated care packages for patients who present with advanced disease or present well; and differentiated care packages for both stable and unstable PLHIV on ART for at least 12 months

With respect to ARV regimens, the 2016 guidelines maintain TLE600 as the preferred first-line regimen for adolescents and adults and extends its use to children ages three years and up who weigh at least 35 kilograms (a change from the 2014 guidelines update, which restricted use of TLE600 to children ages 10 to 14 years). DTG is recommended as an alternative ARV for PLHIV above 15 years of age and unable to tolerate EFV (severe central nervous system (CNS) side effects or moderate-severe rash) or with a history of mental illness. The guidelines also incorporate a special update relating to PV. With respect to viral load monitoring, the guidelines maintain viral load as the test of choice for monitoring response to ART and identifying treatment failure, and recommends routine viral load testing at six months and 12 months after ART initiation and every year thereafter.

II. Operational Planning and Preparation

Table 3: Operational planning and preparation

<p>BENCHMARK: Accurate projections of ARV demand exist at the national and sub-national levels</p> <p>JUSTIFICATION: A national ARV supply plan exists, there are regular coordination meetings to adjust the plan as needed, and routine data needed to inform forecasting and quantification flows directly from ART facilities to NASCOP and KEMSA in a timely and reliable manner.</p>	<p>NEED RATING: LOW</p>
<p>BENCHMARK: ARV drugs are distributed and managed such that supply interruptions and expiries are minimized</p> <p>JUSTIFICATION: KEMSA places advance orders of new ARV products to verify suppliers' capacity to deliver them on time and in full. KEMSA and NASCOP have a strong track record with respect to on-time distribution and commodity security. However, last-mile distribution and supply tracking between ordering facilities and satellite sites need to be strengthened.</p>	<p>NEED RATING: MODERATE</p>
<p>BENCHMARK: Product introduction timing and phasing is strategic and data driven</p> <p>JUSTIFICATION: NASCOP utilizes available clinical and programmatic data — both global and local — to inform the phasing and pacing of new product introduction. The eligibility criteria for transitioning patients to DTG singles are consistent with global norms and guidance.</p>	<p>NEED RATING: LOW</p>
<p>BENCHMARK: Comprehensive transition planning readiness</p> <p>JUSTIFICATION: Capacity for transition planning is high and NASCOP expects to set targets for the share of patients to be transitioned when new drugs or regimens are introduced. However, the complexity of ARV regimen splits, combined with the ongoing implementation of new treatment guidelines, means that providers at lower-level facilities will require additional support and guidance.</p>	<p>NEED RATING: MODERATE</p>

Forecasting and quantification:

Each year, the NASCOP-led Commodity Security Committee (CSC), comprised of the GoK, PEPFAR implementing partners, civil society and county and health facility representatives, coordinates an ARV forecasting and quantification exercise to guide procurements by the three major buyers — Global Fund, PEPFAR and the GoK — over a three-year horizon. However, when a decision has been made on the introduction of a new ARV or other changes in ART recommendations, the commodity team is consulted to ensure that procurements take into account existing stocks, consumption rates as well as the anticipated timeline for availability and uptake of new ARVs. A Commodity Procurement Planning Committee (CPPC), made up of buyers, NASCOP, CHAI and KEMSA, reviews and updates procurement plans each month and reports back to the CSC. The national ARV Technical Working Group (TWG) compiles routine data on supply levels from all 47 counties and produces a monthly commodity stock status report for the CSC with up-to-date information about:^{xiii}

- Adult and pediatric ART enrollment vis-à-vis national targets;
- First- and second-line patient distributions by regimen type (with regimens grouped by NRTI backbone);
- Rate of scale-up for newly introduced ARVs (e.g. atazanavir/ritonavir (ATV/r) and DTG);
- ARV product quantities (in months of stock) located at facilities, stored at KEMSA, or on order;
- Quantities of ARV products (in packs and months of stock) scheduled to arrive in the coming month; and
- A list of any ARV products (regimen, formulation and quantity) at risk of stock-out or expiry.

Tendering and procurement:

Due to differences in buyer tendering and procurement policies (PEPFAR requires FDA approval; Global Fund and GoK require WHO pre-qualification), KEMSA manages Global Fund and GoK procurements, while PEPFAR procurements are managed independently by the Procurement and Supply Management (PSM) project. As a procurement agent, KEMSA with NASCOP, CHAI, and USAID negotiates some of the lowest ARV prices in the world, and has a strong record of in-full, on-time order deliveries from suppliers, a fact KEMSA leadership attributes to the high volume of drugs procured.

During ARV transitions, CPPC advises clinical teams at NASCOP on optimal pacing of procurement to minimize the number of health facility visits for patients, allowing for multi-month prescriptions, and ensuring full utilization of existing ARV stocks. Before the first consignment of a new ARV product arrives in Kenya, CPPC carefully

monitors available and pipeline stock quantities vis-à-vis projected new patient enrollment to ensure that orders are synchronized with demand and a transition strategy is in place. With input from NASCOP, CPPC has already begun to curtail orders of TLE600 and various other ARVs in anticipation of the introduction of TLD FDC. An initial order of one million packs of TLD FDC was placed in September 2017, with additional orders to follow once supplier capacity to deliver is confirmed.

As a procurement agent, KEMSA with NASCOP, CHAI, and USAID negotiates some of the lowest ARV prices in the world, and has a strong record of in-full, on-time order deliveries from suppliers.

Supply management and distribution:

When ARV products arrive in country, KEMSA stores them at its central warehouse and ensures their timely distribution to health facilities across the country. Both consumption monitoring and forecasting is done on a monthly basis as advised by NASCOP. By the 10th of each month, more than 400 “ARV ordering” health facilities submit a combined consumption report and replenishment order to NASCOP for their own sites as well as their satellite sites that draw their stock from ordering facilities. NASCOP reviews the submissions and forwards validated ARV orders to KEMSA’s logistic management unit, which assembles orders, maps out routes, and issues waybills to transport contractors, who deliver ARVs to ordering facilities by the end of the same month. On time, in-full delivery is the norm, and local ARV stock-outs are rare.

Last-mile distribution is the weakest link in the supply chain. Satellite sites are responsible for picking up their ARV products from their ARV ordering facility; however, there is no mechanism in place to track ARV products from ordering facilities to the satellites. NASCOP and KEMSA are in discussions about adapting the distribution system to deliver directly to all (approximately 4,300) ART sites, but no formal decision had been reached as of September 2017.

During the phase-out of d4T, transition pacing posed a challenge for KEMSA. Initially, patients were switched from d4T to other regimens more slowly than anticipated. However, following review of transition data, NASCOP released a communication directing

xiii. Interview with Celia Ngetich, Deputy for PV, AMPATH.

facilities to accelerate the phase-out of d4T. This accelerated pace resulted in expiry of unused stocks of d4T, which then had to be destroyed. Supply chain reliability and performance have improved dramatically since the phase-out of d4T, and both KEMSA and NASCOP anticipate a smooth introduction for TLD FDC. However, clear and concrete transition guidance for providers and stock managers — especially those at lower-level facilities — will be essential.

Use of global and local data and evidence to inform timing and phasing of product introduction:

Kenya has established a track record as an early adopter of optimized ARV products. In determining the timing and phasing of new products, NASCOP and the national TWG look to WHO Guidelines as well as additional local and regional evidence from clinical trials and demonstration projects. In keeping with the global evidence and recommendations, Kenya is currently prioritizing the use of DTG 50mg singles for three patient populations: 1) New and current ART patients exhibiting EFV intolerance; 2) PWID, including those initiating or continuing ART; and 3) patients requiring or currently on third line ART.

With respect to the wider introduction of DTG-based regimens when the FDC of TLD is available, at the time of this assessment NASCOP had not yet issued operational guidance regarding prioritization of specific patient populations. However, NASCOP and other members of the national TWG are carefully tracking emerging safety data on DTG during pregnancy, as the drug's ability to rapidly suppress viremia could be extremely beneficial for prevention of mother-to-child transmission (Kenya's current guidelines do not endorse the use of DTG in pregnancy).

Comprehensive transition planning readiness:

Technical and operational capacity to plan ARV transitions is strong. NASCOP has successfully engineered two major first-line transitions to date. The phase-out of d4T from 2010 to 2012 (wherein adult patients were switched to either ZDV + 3TC + NVP [ZLN] or TLE600), and the phase-in of TLE600 as preferred first-line regimen starting in 2014. During the phase-out of d4T, NASCOP developed an algorithm to guide phase-out and conducted intensive monitoring of stocks so that it could inform health facilities when switching patients was mandated. With respect to a future transition to TLD, NASCOP intends to supplement these approaches with establishment of monthly regimen-specific targets at the national, county and sub-county levels.

One factor Kenya will have to consider carefully in planning for the introduction of TLD is an already-complex ARV regimen landscape. Unlike some countries where the majority of first-line adults and adolescents receive TLE600, Kenya maintains significant numbers of adult patients on four first-line regimens and six second-line regimens (see p. 6). The ongoing introduction of DTG 50mg singles and implementation of the new care and treatment guidelines add another layer of complexity to this landscape. In this context, it is critical that Kenya's future transition plans include clear operational guidance to stock managers and providers regarding not only the phase-in of TLD, but the phase-out of other ARV regimens and how these regimen changes will interface with other changes to care and treatment norms (for example, an intensified focus on pharmacovigilance and multi-month prescribing).



III. Service delivery support

Table 4: Service delivery support

<p>BENCHMARK: Updated directives and training, supervision and data collection tools</p>	<p>NEED RATING: LOW</p>
<p>JUSTIFICATION: The MoH Circular on DTG 50mg singles contains clear and appropriate guidance for county health management teams and healthcare providers. An integrated national training curriculum exists and will be revised based on new ART guidelines. IPs provide multiple forms of complementary site support.</p>	
<p>BENCHMARK: Training and mentorship systems adequately prepare facility-based healthcare workers for transition</p>	<p>NEED RATING: LOW</p>
<p>JUSTIFICATION: Providers possess strong capacity with respect to ART. A national training curriculum covering ART optimization, pharmacovigilance and related subjects has been developed and is being rolled out to all 47 counties. IP reporting to NASCOP on completion of training and mentorship activities at lower-level facilities is uneven and incomplete. IPs underscored the importance of aligning the delivery of newly introduced ARVs to facilities with healthcare worker training and sensitization so that providers can immediately begin prescribing new products once they have been trained.</p>	
<p>BENCHMARK: Community education and demand generation</p>	<p>NEED RATING: LOW</p>
<p>JUSTIFICATION: Treatment literacy among PLHIV is high, and information about newly available drugs travels quickly through media and other channels. In past transitions, patients have learned of new regimens via the media, clinical channels, and civil society organizations, while community outreach and education has lagged behind.</p>	



Transition directives and implementation tools:

MoH routinely issues directives, called circulars, to county health management teams informing them of the essential changes contained in the recently updated national ART guidelines. A sample directive pertaining to the introduction of DTG 50mg singles appears in Appendix 3; it communicates critical information about DTG and how it should be used in a clear and straightforward manner, while reiterating the importance of reporting ADR to both NASCOP and PPB.

In addition to issuing directives, NASCOP and its partners support transition implementation through a number of additional pathways and tools: the national training cascade; supervision and mentorship; job aids including informational flyers, dosing wheels, and algorithm charts; and a NASCOP-led call center — Uliza — offering real-time expert assistance to medical officers, clinical officers and nurses with questions about patient care.

Training and supervision resources and requirements:

Stakeholders conveyed a high level of confidence in provider capacity to transition patients to DTG-based regimens in line with MoH directives, given appropriate training and support. NASCOP is currently leading a national effort to train healthcare workers from ART ordering sites in all 47 counties on ARV optimization. The training curriculum includes the following modules: use of DTG 50mg; use of TLE400 (for Nairobi County only); use of lopinavir with ritonavir (LPV/r) oral pellets as well as overall pediatric ARV optimization recommendations; pharmacovigilance; identification and management of Immune Reconstitution Inflammatory Syndrome (IRIS); and recording and reporting of commodity data via the web-based national logistics management information system (LMIS).^{xiv,xv}

Support from implementing partners (IP), regional TWGs and county training teams will be critical to disseminating this information by ensuring that providers at lower-level facilities receive continuing medical education (CME), training and other on-site support such as mentorship, supervision, supplemental chart reviews, and other data quality assurance checks. IPs underscored the importance of aligning the delivery of newly introduced ARVs to facilities with healthcare worker training and sensitization so that providers can immediately begin prescribing new products once they have been trained. However, as there are no mechanisms in place for IPs to report to NASCOP on training or mentorship activities, there is limited visibility on the completeness of sensitization activities.

Community education and demand generation:

There are two principal pathways through which information about optimized ARVs is transmitted to PLHIV: 1) through the healthcare system and 2) through PLHIV networks, civil society organizations, and other community support forums.

In future transitions, a shared priority for NEPHAK and NASCOP will be ensuring that patients (especially those enrolled at lower-level and rural facilities) receive timely and consistent information from both community and clinical sources on the rationale for TLD introduction, why certain patient populations are to be prioritized during the phase-in process, and the continuing safety and efficacy of existing ARV regimens.

NEPHAK reported that, during past transitions, some healthcare workers received training or sensitization about new ARV regimens only after the drugs were available locally, such that patients inquiring about new treatment options initially received incomplete or incorrect information.^{xvi}

With respect to the community pathway, NEPHAK disseminates information about changes to treatment standards and regimens via its online newsletter, workshops, presentations to support groups, and group messaging features of social media platforms such as WhatsApp.

In future transitions, a shared priority for NEPHAK and NASCOP will be ensuring that patients (especially those enrolled at lower-level and rural facilities) receive timely and consistent information from both community and clinical sources on the rationale for TLD introduction, why certain patient populations are to be prioritized during the phase-in process, and the continuing safety and efficacy of existing ARV regimens.

xiv. Optimization of ART Regimens. NASCOP Presentation: Sept. 1, 2017.

xv. Kenya takes steps to reduce the risk of treatment disruptions. Aidspace web site. April 5, 2016. Accessed November 1, 2017: http://www.aidspace.org/gfo_article/kenya-takes-steps-reduce-risk-treatment-disruptions.

xvi. Kenya's healthcare worker training system is multi-tiered, relying on regional mentors to convey information to county and sub-county medical officers, who in turn train facility-based healthcare workers. There have been past delays and gaps in transmission of information to lower-level facilities.

IV. Transition monitoring and visibility

Table 5: Transition monitoring and visibility

<p>BENCHMARK: Clinical indicators are monitored closely during the transition period to facilitate appropriate care decisions</p>	<p>NEED RATING: LOW</p>
<p>JUSTIFICATION: Capacity to monitor and analyze clinical indicators is strong at central and tertiary care levels. EMRs currently capture data on 50% of patients nationwide, and recent efforts to link various electronic databases should improve data availability, quality and analysis at the national and county levels, as well as at the facility level for healthcare providers.</p>	
<p>BENCHMARK: Adverse drug reactions are promptly reported and documented</p>	<p>NEED RATING: MODERATE</p>
<p>JUSTIFICATION: A system for reporting ADR exists, and 80% of ADRs reported are related to ARVs of which 80% are reported through the electronic platform. Reporting rates are low and vary significantly across geographic areas. To encourage reporting rates NASCOP has recently integrated a pharmacovigilance module into the ARV optimization training.</p>	
<p>BENCHMARK: Stock monitoring systems allow early detection of stock-out, expiry risks</p>	<p>NEED RATING: MODERATE</p>
<p>JUSTIFICATION: In past transitions, uptake rates have not always matched expectations. Lack of real-time consumption data limits early detection of consumption anomalies. Due to the complexity of the ARV regimens available, close monitoring of consumption of the ARVs is crucial.</p>	



Clinical monitoring:

NASCOP and its partners support a number of advanced electronic health information systems and dashboards, including a centralized national data warehouse, several electronic medical record (EMR) systems (covering 50% of all ART patients), a laboratory information system (LIS) with corresponding early infant diagnosis and viral load dashboards, and an ARV dispensing tool (ADT). The national data warehouse captures data elements recorded in the ART patient card (the “green card” or MoH Form 257) and aggregates these to allow generation of cross-sectional and cohort reports on key patient outcomes (including by ART regimen). In addition, a newly established enhanced data system (EDS) will link data from multiple EMR systems, the ADT, LIS, and other databases via an interoperability layer, allowing NASCOP and its partners to access a comprehensive dataset on patient outcomes including side effects and viral load suppression at health facilities throughout the country. The EDS will be a valuable asset for intensified patient monitoring during the transition to TLD, but focused training and supervision will be needed to fully realize its potential at all levels of the health system.

Pharmacovigilance:

The PPB is responsible for managing PV activities in Kenya. The PPB offers healthcare workers two options for submitting reports of ADR: a paper-based “yellow form” and a web-based tool. The web-based tool can be accessed using the following link: <http://www.pv.pharmacyboardkenya.org/sadrs/add>.

In a typical month, PPB receives around 150 reports of ADRs, of which approximately 80% are related to ARV drugs. This rate is well below the WHO optimal standard of >200 reports per year per million inhabitants^{xvii} and suggests that many cases of ADR are going unreported. There are multiple issues resulting in low reporting rates including limited understanding by healthcare workers on the importance of reporting and how the information will be used by the program because feedback from PPB following submission of a report is not routinely provided to healthcare workers. Officials noted significant geographic variations in PV reporting rates, with Nairobi County reporting most consistently, followed by Uasin Gishu, Kiambu and Vihiga counties; other counties have substantially lower reporting rates. Approximately 80% of PV reports are submitted via the web-based reporting tool, while only 20% are submitted in hard copy. One major advantage of the electronic interface is that it provides automated confirmation of each case submitted. In addition, PPB occasionally provides supplemental feedback to the reporting facility to indicate whether an investigation has been opened.

Two efforts are currently underway to strengthen PV in Kenya. The first effort, led by PPB, focuses on enhancing the functionality of the web-based system, such that PPB can collect additional details

about products linked to ADR (e.g. manufacturer and batch number), provide more nuanced feedback to health facilities, and easily share relevant PV data with the appropriate MOH program managers (for instance, NASCOP staff could receive regular reports on any ADR reported for ARV drugs). The second effort, led by NASCOP with support from the OPTIMIZE project, is a PV demonstration project at 24 health facilities to support enhanced monitoring, reporting and analysis of AEs during the introduction of DTG. An overview of this project appears on the next page.

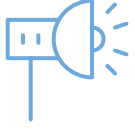
Stock monitoring:

The CSC, in collaboration with county and facility-based stock managers, is responsible for monitoring ARV stock levels to prevent stock-outs, expiries and waste. Two factors limiting the CSC’s ability to effectively detect and respond to consumption anomalies early are 1) lack of real-time data on ARV stock levels, and 2) “invisibility” of stocks after they are dispatched from ordering facilities to satellite sites. Despite these limitations, the CSC has developed a rigorous stock monitoring system built on routine analysis and visual representations of monthly ARV stock data based on reports from ordering facilities, which compile consumption data and replenishment orders from their own pharmacies and satellite sites and convey these to the CSC.



Georgina Goodwin

xvii. Ribeiro-Vaz, Inês, Santos, Cristina Costa, and Cruz-Correia, Ricardo. (2016). Promoting adverse drug reaction reporting: comparison of different approaches. *Revista de Saúde Pública*, 50, 14. Epub May 03, 2016. <https://dx.doi.org/10.1590/S1518-8787.2016050006122>



SPOTLIGHT ON PHARMACOVIGILANCE AND TOXICITY MONITORING FOR ADVERSE DRUG REACTIONS:

When the WHO first recommended the phase-out of d4T due to toxicity, some national stakeholders were reluctant to adopt this recommendation due to lack of local documented/reported evidence on d4T-related toxicity. If Kenya had had a robust PV system in place — with corresponding data on ADRs — the phase-out of d4T may have started earlier and proceeded more rapidly.

A rapid analysis of Kenya’s PV system vis-à-vis the four optimization domains yields mixed findings:

1 — ENABLING ENVIRONMENT (POLICY)

While a national pharmacovigilance policy and guidelines exist, they are applied inconsistently across counties and health facilities, with the most consistent application occurring among the handful of health facilities that served as sentinel sites for the WHO-sponsored ARV-related ADR surveillance project nearly a decade ago.

2 — PLANNING AND PREPARATION (TOOLS AND PROCESSES)

Field-tested PV tools exist in both paper and electronic formats, and paper-based tools appear to be widely available at health facilities. Paper tools include the “yellow form” for reporting suspected ADR, including congenital anomalies, the “pink form” for reporting poor-quality medicinal products, and Patient alert cards for patients (on hypersensitivity of a drug). The electronic reporting form may be used by any category of healthcare worker (including community health workers) as well as by patients and their family members. The yellow form lacks a field allowing the reporting party to specify the manufacturer of the drug or drugs associated with an ADR, though this field is included in the pink form.



3 — SERVICE DELIVERY SUPPORT (HEALTHCARE WORKER READINESS)

Despite the existence of a well-defined system and tools, most health facilities and providers do not routinely submit reports of suspected ADRs, and those that do submit with regularity do not always receive timely or useful feedback from PPB. In the absence of recent PV training and consistent feedback, many healthcare workers lack the incentive or confidence to submit or follow up on cases of ADRs. In addition, a PV pilot supported by AMPATH found that ART patients might hesitate to share information about ADRs with their provider (whereas they were more willing to share this information with peer educators^{xii}); this indicates that an adapted approach may be needed to capture accurate data on the rate of ADRs.

As Kenya looks ahead to the introduction of TLD FDC, it is important to have a strong PV system in place. DTG has been well studied in clinical trials and healthcare settings in the US and Europe, but data on DTG-related adverse events (AEs) and toxicity is limited in real world public health settings in sub-Saharan Africa. As there have been observational reports of treatment-limiting neuropsychiatric effects and concern about IRIS with use of DTG, it is essential that the rollout of DTG in Kenya be accompanied by close monitoring to identify concerning signals early on. Post-market surveillance and systematic AE reporting for DTG will also be important for programmatic planning purposes; incidence of AE in different patient populations and geographic regions can help inform the phasing and pacing of scale-up of DTG-based regimens.

With leadership from NASCOP, other PEPFAR-supported implementing partners and the Clinton Health Access Initiative (CHAI), Kenya is planning to pilot enhanced monitoring for ADRs at 24 health facilities transitioning patients to DTG-based regimens, with the aim of scaling this approach nationally over time. This demonstration project which will begin in late 2017 presents a unique opportunity to support enhanced patient monitoring while strengthening the national PV system.

Participating health facilities will use their existing data systems as well as a newly developed symptom checklist to gather information about ARV-related side effects that patients experience (including type and severity). In addition, providers will record data on side effects (and any resulting regimen changes) in patient files and report any ADR to PPB via the manual ADR reporting form (Yellow Form) or web-based reporting tool. AE data recorded in electronic patient files via IQCare, "Kenya EMR" and "Open MRS" will be aggregated across health facilities and geographic areas on a monthly basis to facilitate comparison and triangulation of ADR data reported to PPB and recorded in patient files.

The findings of the enhanced PV demonstration project will be used to inform guidance for healthcare providers and patients during the national scale-up of TLD, and to strengthen PV training and support strategies.

xii. Interview with Celia Ngetich, Deputy for PV, AMPATH.

4 — MONITORING AND VISIBILITY

At the national level, there are gaps in the use of ADR data that are submitted to PPB; data are not effectively aggregated and made accessible to all actors (e.g. NASCOP and other disease-specific programs), and there is no well-defined protocol to guide national response when ADRs for a given drug exceed an expected threshold.



Casey Kelbaugh

Recommendations:

- 1** — Develop comprehensive guidance on preferred first, second and third-line ART regimens, with a view to simplification and streamlining.

Comprehensive technical guidance will be needed on eligibility for TLD, how to transition and which regimen(s) should be prescribed for patients who cannot tolerate or who experience treatment failure on TLD

- 2** — Communicate transition information and guidance to Healthcare workers and patients at lower-level health facilities through multiple channels.

- To ensure that phasing and pacing of TLD introduction comply with the transition plan currently under development, NASCOP and its partners, including NEPHAK, should consider developing and implementing a targeted communication plan to promote transition awareness and understanding among providers, stock managers and PLHIV.

- 3** — Strengthen PV and toxicity monitoring.

- Leveraging the PV guidance in the 2016 national treatment guidelines and the PV electronic reporting platform for ADR, NASCOP should define a strategy to strengthen PV systems for assessing ADR in patients transitioning to optimized ARVs, with an emphasis on identifying PV best practices that can be applied throughout the country.
- Dedicated training and/or on-the-job mentorship may be needed to increase uptake and use of the PV electronic reporting platform.
- Implement innovative approaches like use of peer educators to extract information on ADR from PLHIV.
- PPB should strengthen collaboration with various MOH programs such that system enhancements benefit all end users of PV data.



Appendix 1: List of Interviewees

Date	Name	Title	Organization
8th September 2017	Mr. John Kabuchi	Procurement Manager	KEMSA
	Mr. Nelson Otwoma	National Coordinator	NEPHAK
	Dr. Angela Mc'Ligeyo	Sr. Technical Advisor	CHS
	Dr. Susan Njogo	HIV Commodity Management	NASCOP
11th September 2017	Jackson Hungu	Deputy Country Director	CHAI
	Dr. Laura Oyiengo	Pediatric and Adolescent	NASCOP
	Dr. Jacob Odhiambo	Clinical Advisor and Deputy Project Director, Kenya HMIS Project	Palladium Group
12th September 2017	Mr. Isaac Mwele	Distribution Officer	KEMSA
	Dr. Jared Mecha	Principal Investigator	CRISSP
13th September 2017	Dr. Alexandra Vandenbulcke	Country Medical Coordinator	MSF - France
	Dr. Abraham Katana	Treatment and Care Branch Chief	CDC Kenya
	Dr. Evelyn Ngugi	Deputy Treatment Branch Chief	CDC/Kenya
14th September 2017	Dr. Edwin Burugu	Product Evaluation and Registration	PPB
	Dr. Christabel Khaemba	Head of Pharmacovigilance	PPB
18th September 2017	Prof. Sylvester Kimaiyo	Executive Director	AMPATH (Eldoret)
	Mercy Maina	Pharmacist/Mentor	AMPATH
	Celia Ngetich	Deputy, Pharmacovigilance	AMPATH
	Sheila Masit	Data Manager	AMPATH
19th September 2017	Emmanuel Amadi	Data Manager	ICAP (Siaya/Kisumu)
	Dennis Atande	Data Manager	ICAP (Siaya/Kisumu)
	Gladys Omboi	Program Officer	ICAP (Siaya/Kisumu)
	Dr. Rukia Aksam	Medical Officer in CCC	JOOTRH
20th September 2017	Dr. Maureen Kimani	Head of Treatment and Care	NASCOP
	Dr. Irene Mukui	Former Head of Treatment and Care	NASCOP

Appendix 2: Questionnaire

OPTIMIZE

Protocol #: AAAR0260

OPTIMIZE: Interview Guide

Interviews will be structured around the following core areas (shown below with corresponding illustrative questions):

1. Overall:

- *In a recent global stakeholder assessment conducted by ICAP¹, 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? 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 had fulfillment challenges in the past*
 - *Limited awareness of optimal ARV drug availability and benefits among recipients and health care providers*
 - *Poor visibility of ARV drug stocks at the decentralized level, leading to facility-level stock-outs*
- *What are additional barriers to introduction and scale-up of the potential new optimized ARVs? What approaches could be taken to reduce these barriers?*
- *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?*

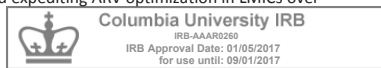
2. Enabling environment (policy, advocacy & finance):

- *Is there a regular schedule/cycle for country ARV tenders? When is the next tender process scheduled? 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 timeline for incorporating a new product into the national treatment guidelines? Which entity/entities wield the most influence in this process? To what extent to WHO Guidelines influence the decisions/recommendations of these entities? What data or evidence is recommended or required?*
- *How is information about optimized ARV products communicated to clinicians, patients, and other groups? What additional advocacy activities/efforts would be beneficial? Who is best placed to implement this? What lessons are there from past advocacy efforts to build on (e.g. when shifting to FDCs)?*
- *What is the typical timeline and process for registering a new ARV product in country? Has the NDRA utilized the WHO Collaborative Registration Procedure for any ARVs? If so, for which? If not, are there plans for the NDRA to utilize the CRP for ARVs in the future? Why or why not?*

3. Planning & preparation:

- *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 advanced procurement practices have been adopted/utilized (pooled procurement, coordinated procurement, multi-year agreements)? Are there plans to adopt other advanced*

¹ 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.



OPTIMIZE

Protocol #: AAAR0260

procurement practices, and if so, when? What is the process and timing for adding new ARV drugs to the procurement and distribution systems?

- *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?*
- *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?*
- *In past transitions, has there been a formal communication plan? A formal M&E plan? How has communication of roles and responsibilities been handled?*
- *Are there particular planning tools that will be used for the transition?*

4. Service delivery support:

- *What supplemental training, mentoring or supervision has been provided to clinicians during major ARV transitions in the past? What types of supplemental service delivery support would be most helpful for future transitions?*
- *What types of tools (SOPs, job aids, etc) have been developed and utilized to facilitate past ARV transitions?*
- *What is national policy on multi-month ARV prescriptions? Differentiated service delivery models? How will these be integrated into transition planning?*
- *What are the various pathways through which patients are prepared for regimen switches? Which of these have been most effective?*

5. Transition monitoring & visibility:

- *What M&E processes, systems and tools have been used during past ARV transitions? For patient monitoring and management? Cohort analysis? Stock monitoring and reporting? Tracking of progress against transition targets?*
- *What types of QA and QI activities have been implemented to support successful ARV transitions? What additional QA and QI approaches would be useful for future transitions?*

6. Early adopter research:

- *Have operations research /implementation science studies been carried out focusing on any of the following topics:*
 - *Effect of patient characteristics and service delivery models on patient outcomes*
 - *Market behaviors (uptake, acceptability, willingness to pay) among patients, providers and procurers*
 - *Monitoring of birth outcomes, including congenital anomalies, prematurity, etc via surveillance systems or birth registries*
 - *Factors in maximizing product uptake by patients, providers*
- *If not, which of the above topics would be the most pertinent/beneficial for upcoming ARV transitions?*



Appendix 3: MoH Circular on DTG Singles



**MINISTRY OF HEALTH
OFFICE OF THE DIRECTOR OF MEDICAL SERVICES**

Telephone: Nairobi 254-020-2717077
Fax: 254-2719008
Email: dmskenya@gmail.com

AFYA HOUSE
CATHEDRAL ROAD
P. O Box 30016-00100
NAIROBI

When replying please quote:

Ref: MOH/NASCOP/ART/05

Date: 8th June 2017

All County Chief Officers of Health

Thro'

The Chairman
Council of Governors
Delta Plaza



RE: INTRODUCTION OF DOLUTEGRAVIR (DTG) AND RECOMMENDATIONS FOR ITS USE IN HIV TREATMENT

The Ministry of Health has continued to provide policy and guidelines on HIV prevention and treatment in Kenya. The Guidelines on use of Antiretroviral Drugs for Treating and Preventing HIV infection in Kenya launched in July 2016 provides guidance for introduction of efficacious and user friendly ARVs as they become available in the market. Tenofovir/Lamivudine/Efavirenz (TLE) is the preferred first line treatment in adolescents > 12 years and adults weighing over 40 kgs.

DTG an integrase strand transfer inhibitor (INST) that has become available in national ARV supply chain. DTG is available as a single formulation of 50mg taken once daily by adolescents > 12 years and over 40kgs and adults.

It is recommended for use in the following situations:-

1. Alternative regimen for PLHIV with EFV intolerance.
2. All People Who Inject Drugs (PWIDs) on ART or initiating PWID on ART.
3. For constituting third line regimen for PLHIV with failing PI based second line regimen.



It will be used in combination with dual fixed dose combination of TDF/3TC as an alternative regimen for PLHIV with EFV intolerance, PWID on ART and for constituting third line regimen for PLHIV failing second line PI based regimen.

NB: It is **NOT** recommended in pregnant and breastfeeding women, TB/HIV co-infected patients and in children < 12 years or < 40kgs due to limited safety and efficacy data. More information on DTG can be obtained from www.nascop.or.ke.

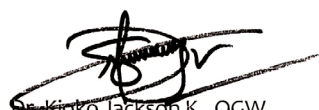
Dosage

Alternative first line regimen in cases of EFV intolerance or for People Who Inject drugs (PWID)

TDF 300MG/3TC 300MG + DTG 50MG
TWO PILLS ONCE A DAY

The purpose of this circular is to notify you of availability of DTG 50mg for the specific indications highlighted in the guidelines 2016 and to request that this information is shared with HIV service providers in public and mission facilities. DTG should be ordered and reported through the national ARV supply chain. Medication, education and counseling to ensure a smooth transition to DTG. An active identification and reporting of any adverse drug reaction should be done promptly and reported to both PPB and NASCOP.

For further clarification, kindly contact Dr. Maureen Kimani, 0721587511; maureen.nyambura@gmail.com or Dr. Susan Njogo, 0722 419865; smnjogo2012@yahoo.com.



Dr. Kioko Jackson K., OGW
DIRECTOR OF MEDICAL SERVICES



Appendix 4: September 2018 Addendum

The analysis and recommendations presented in this assessment were based on available information as of September 2017. At that time, Kenya was planning to implement tenofovir (TDF), lamivudine (3TC) and dolutegravir (DTG) as the preferred first-line regimen for all populations including existing patients on first-line legacy regimens. However, since then, new data about DTG has become available which impact the findings and recommendations from this assessment. This addendum has been prepared to provide an update on the current country plan to optimize ART including changes to populations eligible for DTG and plans for monitoring use of optimized ARVs

In May 2018, preliminary data from an observations study in Botswana noted a potential increased risk of neural tube defects (NTDs) in women with peri-conception exposure to DTG. Currently, data are limited and it is unclear if this finding represents a true increased risk of birth defects with peri-conception exposure to DTG. Outcomes from ongoing pregnancies being monitored in Botswana will provide additional information to determine the level of risk by mid-late 2019. However, in response to this early data, international advisories on the potential risk of NTDs were issued by multiple agencies including the United States Food and Drug Administration (USFDA), the World Health Organization (WHO) and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). This was taken into consideration by the Government of Kenya (GoK) in developing a revised plan for the introduction of DTG-containing regimens.

2018 Kenyan ART guidelines considerations

Consultations were held with stakeholders to develop a national position on the use of DTG-containing regimens in women and adolescent girls of childbearing potential. As a first step, the Ministry of Health issued an advisory on the use of DTG in women of childbearing age (see Annex 1). Stakeholders agreed to amend the guidelines to include new concerns about the use of DTG in women and adolescent girls of childbearing potential. The new guidelines on use of antiretroviral drugs for treating and preventing HIV in Kenya were launched on 22nd August 2018. These guidelines introduced DTG-based regimens as the preferred first-line ART regimen and included the recommendation that DTG-containing regimens may be used in women and adolescent girls of childbearing potential who are on effective contraception.

Management of patients already transitioned to DTG-based ART

At the end of 2017, in order to support the transition process, NASCOP-MOH directed 24 high volume facilities (Table 1) to transition current patients on the suboptimal regimen of TDF/3TC+Nevirapine (NVP) to TDF/3TC+DTG. These patients were expected to transition to the fixed dose combination of TDF, 3TC and DTG (TLD) once it became available.

Table 1: Health facilities for enhanced transition to TLD from TL+N

No.	Name of the health care facility
1.	Eastern Deanery Aids Relief Program (EDARP) St. Vincent
2.	EDARP St. Veronica
3.	EDARP St. Alice
4.	EDARP Soweto
5.	EDARP Shauri Moyo
6.	EDARP Ruai
7.	EDARP Njiru
8.	EDARP Mathare
9.	EDARP Kayole
10.	EDARP Kariobangi
11.	EDARP Huruma
12.	EDARP Donholm
13.	EDARP Dandora
14.	EDARP Babadogo
15.	Siaya County Referral Hospital
16.	Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH)
17.	Machakos County Referral Hospital
18.	Moi Teaching and Referral Hospital (MTRH)
19.	Chulaimbo Hospital
20.	Coast Provincial General Hospital (CPGH)
21.	Kenyatta national Hospital (KNH)
22.	Kitale County Referral Hospital
23.	Nyeri County Referral Hospital
24.	Webuye County Referral Hospital

With revised guidance on DTG use by women and adolescent girls of childbearing potential, the facilities listed above reviewed the profiles of all patients on DTG-containing regimens to identify women and adolescent girls of childbearing potential who had been transitioned to a DTG-based regimen. They also noted identified women who had conceived after transitioning to a DTG-containing regimen. For those non-pregnant women and adolescent girls of childbearing potential without effective contraception, were advised to be transitioned back to efavirenz-based ART.

NASCOP and other stakeholders subsequently carried out a rapid assessment of these facilities to clearly establish the number of women and adolescent girls of childbearing potential on DTG and determine which women conceived while on DTG-containing ART. The report was not yet complete at the time of this writing. NASCOP is also developing a plan to monitor the birth outcomes of all pregnant women including those who have already delivered while on DTG. Plans are in place to share these findings with global stakeholders as they become available.

NASCOP and other stakeholders are also finalizing communication resources for health care providers and educational messages for people living with HIV (PLHIV) on the potential risk of NTD with peri-conception exposure to DTG.

Transition to preferred ART regimen in eligible first-line ART patients

Preferred First-line ART Regimens for Adolescents and Adults

≥ 15 years (or ≥ 35 kg body weight)	TDF + 3TC + DTG or TDF + 3TC + EFV	TDF/3TC/DTG (300/300/50mg): 1 tab once daily or TDF/3TC/EFV (300/300/400mg): 1 tab once daily
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¹ DTG is not currently recommended for women and adolescent girls of childbearing potential because of possible risk of birth defects when DTG is used around the time of conception. Women who are on effective contraception may opt to use DTG and should be supported in their decision.

² Female PWID/HIV of childbearing potential use TDF + 3TC + ATV/r as preferred first-line ART.

In anticipation of transitioning current eligible first-line ART patients to TLD, the MOH has already procured stocks of TLD. Nairobi county and sub-county health management teams, implementing partners, and ARV ordering health facilities have been sensitized on how to transition virally suppressed eligible patients from current regimens of TLE, TL+NVP, TL+DTG, AZT/3TC+EFV/NVP, ATV/r or LPV/r based first-line ART to TLD. Transitioning has already been initiated in Nairobi County. Countrywide initial distribution of TLD will begin in the late fall 2018 to facilitate transition of eligible populations to the preferred first-line ART i.e. TLD. Other adult and pediatric ART regimen transitions will be planned and communicated accordingly based on current ART stocks in country.

The MOH initially had also procured limited stocks of reduced dose EFV in combination with TDF and 3TC (TLE400). Early use of TLE400 was limited to patients in Nairobi health facilities and current stocks of TLE400 are almost exhausted. Based on available evidence on use of TLE400, MOH has now procured TLE400 for countrywide use in populations not eligible for TLD.

ARV Commodity Procurement

Based on the revised recommendations for ART in various populations, ARV forecasting and procurement has been adjusted to avoid stockouts of essential commodities. Routine stocks monitoring and timely procurements are done under the leadership of NASCOP.

Service Delivery Support

Since the guidelines have been launched, an orientation package has been developed for health care worker capacity building. The orientation package focuses on new recommendations through case studies. All required resources needed to support service delivery have been identified and are being finalized. National and regional mentors were oriented on the new guidelines from 5-7th September 2018 using the ECHO platform. ECHO is a knowledge-sharing network that links expert medical teams with primary care clinicians in rural and urban underserved locations. Facility-level continuing medical education will be carried out utilizing innovative approaches and platforms such as ECHO to ensure that the wide range of health care workers are sensitized on new updates of 2018 ART guidelines.

Transition Monitoring and Visibility

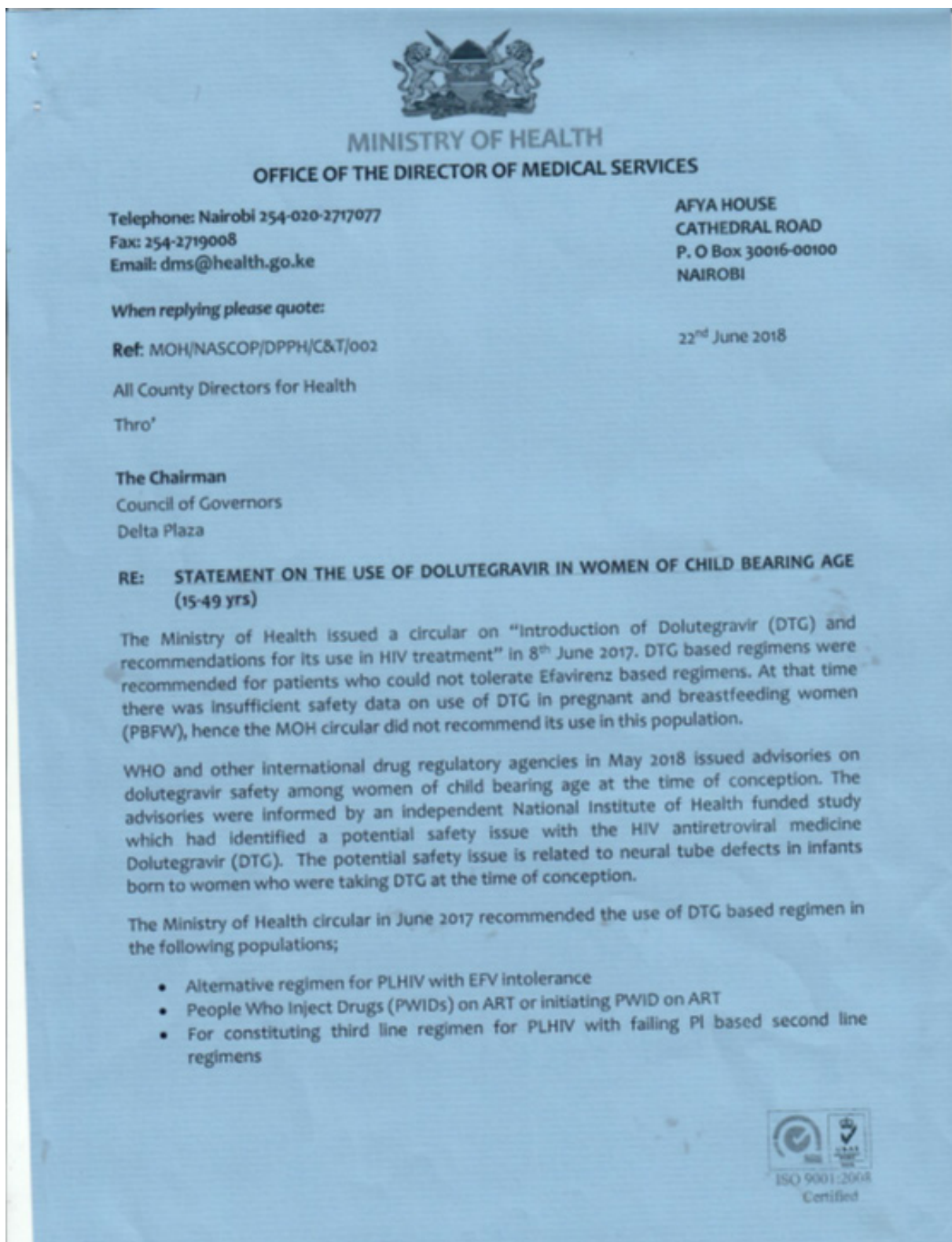
At the national level, the Pharmacy and Poisons Board (PPB) in collaboration with NASCOP is playing a key role in strengthening pharmacovigilance (PV). PV for optimized ARVs has been emphasized in every interaction with health care providers. Sensitization on documentation of adverse drug reactions and PV reporting is integrated in every communication to health care providers.

Additionally pharmacists from the county, sub-county and health facility level as well as pharmacy technical advisors from implementing partners are monitoring stock levels closely and have been authorized to inform NASCOP of potential stock-outs or expiry risks in order to support the development of contingency plans to address any challenges that may arise.

Summary of recommendations:

1. Communicate ART transition information and guidance to health care workers and patients at lower-level health facilities through multiple channels.
2. Strengthen Pharmacovigilance (PV) and ARV toxicity and patient outcome monitoring.

Annex 1: Statement on use of Dolutegravir in women of child bearing age



Annex 2: Guidelines on use of antiretroviral drugs for treating and preventing HIV in Kenya http://www.nascop.or.ke/?page_id=2431



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. USAID is proud to support OPTIMIZE, a global partnership with unifying distinct voices to achieve a common goal: accelerating access to simpler, safer and more affordable HIV treatment.

For further information or to request technical assistance from **OPTIMIZE**, please contact ICAP at optimize@cumc.columbia.edu.



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