Annual ARV Buyer Seller Summit Schedule

Washington, DC, USA | Sunday, November 24, to Wednesday, November 27, 2019

Objective: To engage with industry on improving future demand visibility and improve the structure by which buyers and sellers interact and work together to improve performance and efficiency.

TIME	TOPIC	SPEAKERS	SLIDE LOCATION
Sunday, November 24 (Day 0)			
13:00 to 17:00	**One on One Sessions**		**SECOND FLOOR BREAKOUT ROOMS**
Coffee from 15:30 to 16:00			**SECOND FLOOR FOYER**
Monday, November 25 (Day 1): Forward Demand and Regulatory Matters			
Breakfast and Registration from 7:30 to 8:30			**EAST ROOM**
Morning Plenary from 8:30 to 13:00			
8:30 to 9:00	**Welcome Remarks**	James Maloney, *Division Chief Supply Chain for Health, USAID* Martin Auton, *Senior Manager, Principal Recipient Services, Sourcing and Supply Chain Department, The Global Fund* Khadija Jamaloodien, *Director, Affordable Medicines, National Department of Health, Republic of South Africa*	**SLIDE #4**
9:00 to 10:30	**Individual Highlights for Each Procurement Channel**	KEMSA, Douglas Onyancha Ethiopia PFSA, Tsion Tsegaye Republic of South Africa, Khadija Jamaloodien	**SLIDE #8** **SLIDE #22** **SLIDE #36**

TIME	TOPIC	SPEAKERS	SLIDE LOCATION
9:00 to 10:30	**Individual Highlights for Each Procurement Channel**	UNDP, Zafar Yuldashev Global Fund, Uranchimeg Badarch GHSC-PSM, Alan Pringle	**SLIDE #53** **SLIDE #66** **SLIDE #82**
Coffee from 10:30 to 11:00			**STATE FOYER**
11:00 to 11:30	**Five Year WHO-AMDS Forecast**	Boniface Nguimfack, WHO Dr. Adebiyi Adesina, Avenir Health	**SLIDE #92**
11:30 to 13:00	**FDA Presentations** 1-CRP Lite Overview 2-Multi Month Dispensing (MMD) and Shelf Life Extension 3-Review of FDA Responses to Questions from ARV Stakeholders	Dr. Harinder Chahal, USFDA Dr. George Lunn, USFDA Dr. Peter Capella, USFDA Dr. Sarita Boyd, USFDA, Dr. David Araojo, USFDA William Lewallen, USFDA	**SLIDE #113** **SLIDE #125** **SLIDE #147**
Lunch from 13:00 to 14:00			**EAST ROOM**
14:00 to 18:00	**One on One Sessions:** The Global Fund, Republic of South Africa, USAID, GHSC-PSM, KEMSA, Ethiopia PFSA, UNDP, PAHO		**SECOND FLOOR BREAKOUT ROOMS**
Coffee from 15:30 to 16:00			**SECOND FLOOR FOYER**
Tuesday, November 26 (Day 2) - Quality Assurance and Product Optimization			
Breakfast from 8:00 to 9:00			**EAST ROOM**
Morning Plenary from 9:00 to 12:00			
9:00 to 9:30	**Quality Assurance: Expectations and Analyses**	Dr. Christine Malati, USAID (PEPFAR) Dr. Aida Cancel, GHSC-QA Hien Dinh, GHSC-QA Martin Auton, Global Fund	**SLIDE #154** **SLIDE #165**
9:30 to 10:00	**Updates on Medicines 4 All**	Dr. Eugene Choi, Virginia Commonwealth University	**SLIDE #166**
Coffee from 10:00 to 10:30			**STATE FOYER**
10:30 to 12:00	**Future Guidelines and Treatment Optimisation**	Martin Auton, Global Fund and PAC co-chair Dr. Marco De Avila Vitoria, WHO Dr. George Siberry, USAID (PEPFAR) Dr. Hilary Wolf, U.S. Department of State (PEPFAR)	 **SLIDE #195** **SLIDE #238** **SLIDE #261**

TIME	TOPIC	SPEAKERS	SLIDE LOCATION
		Wesley Kreft, ARV Procurement Working Group	**SLIDE #279**
Lunch from 12:00 to 13:00			**EAST ROOM**
13:00 to 18:00	**One on One Sessions:** The Global Fund, Republic of South Africa, USAID, GHSC-PSM, KEMSA, Ethiopia PFSA, UNDP, PAHO		**SECOND FLOOR BREAKOUT ROOMS**
Coffee from 15:30 to 16:00			**SECOND FLOOR FOYER**
Wednesday, November 27 (Day 3) – Supply Chain Optimisation			
Breakfast from 8:00 to 9:00			**EAST ROOM**
9:00 to 10:00	Grand Ballroom available for use for side meetings.		GRAND BALLROOM
Coffee from 10:00 to 10:15			**STATE FOYER**
Morning Plenary 10:15 to 12:30			
10:15 to 10:45	**18 Month Consolidated Forecast**	Chirag Rajpuria, The Global Fund	**SLIDE #288**
10:45 to 12:15	**Supply Chain Optimisation and Country Uptake**	Dr. Messai Belayneh, USAID (PEPFAR) Dr. Christine Malati, USAID (PEPFAR) Khadija Jamaloodien, Republic of South Africa Charles Lwanga, USAID|Kenya (PEPFAR) Mercy Mpatwa, United Republic of Tanzania Dr. Nagesh Borse, GHSC-PSM	**SLIDE #311** **SLIDE #338** **SLIDE #365** **SLIDE #382** **SLIDE #392**
12:25 to 12:45	**Closing Remarks**	Martin Auton, Global Fund Khadija Jamaloodien, Republic of South Africa Dr. William Paul, US Department of State (PEPFAR)	GRAND BALLROOM
Lunch from 12:45 to 14:00			**EAST ROOM**
14:00 to 17:00	**One on One Sessions:** The Global Fund, Republic of South Africa, USAID, GHSC-PSM, KEMSA, Ethiopia PFSA, UNDP, PAHO		**SECOND FLOOR BREAKOUT ROOMS**
Coffee from 15:30 to 16:00			**SECOND FLOOR FOYER**

ARV Buyer Seller Coordinated Demand Visibility Update

November 2019
Washington, DC

The Global Fund

PEPFAR

Republic of South Africa

Global Fund, PEPFAR, Governments of South Africa and Kenya are working together to improve the consolidated demand outlook

What we will do

Coordinated approach and messages

Synergistic strategies

Direct engagement with suppliers & supplier visits (sometimes)

Align on **key supplier performance metrics**

Sharing of **synthesized market intelligence** and general supplier performance

Sharing information (without providing confidential / sensitive information)

Providing **improved demand visibility**

What we will not do together

Long-term agreements with manufacturers

Selection of suppliers and demand allocation

Execution of **purchase orders**

We will not manage actual **supplier performance jointly**

Managing **overall supplier performance** (Price, lead-time, delivery etc.)

Increased dialogue between buyers & sellers over the past 5 years

- All updated 18 month forecasts are posted @ https://www.theglobalfund.org/en/sourcing-management/health-products/antiretrovirals/
- Looking at larger issues to increase efficiency (packing, data visibility, dialogues on current concerns and appreciated actions)
- A number of procurement channels considering performance metrics, Framework contracts and moving away from frequent spot tenders
- Big funders/buyers committed to further strengthen partnership and improve on demand management

Large ARV Buyers and Sellers Forum November 2018 (Mumbai)

Key Take-Aways and Discussion Points

Topics discussed

ARV Transitions are Occurring at a Rapid Rate	▪ Noted that the past transitions have taken 4 to 5 years to be completed, whereas current ARV transitions are expected to be completed much faster ▪ This has led to shorter production life cycles for ARVs, down to 3 years and less in some cases.
Accuracy and Demand Visibility	▪ Agreement to share more analysis on forecast accuracy ▪ Looking to share more firm demand for new ARVs that are required for optimization efforts ▪ Interest in sharing more data to show the decrease or “phase-out” of legacy ARVs that are being replaced
Interest in Ensuring Decreasing Shelf-Life Requirements for Importation	▪ Participants agreed that efforts are needed to reduce shelf-life requirements for the importation of ARVs ▪ This will increase supply chain efficiency and flexibility; and regularity of deliveries ▪ Further, this could help incentivize countries to ensure lean and efficient in-country supply chains, and reduce high buffer stock levels, which may limit ARV transition efforts

ARVs Large Buyers/Sellers Forum

Kenya Presentation

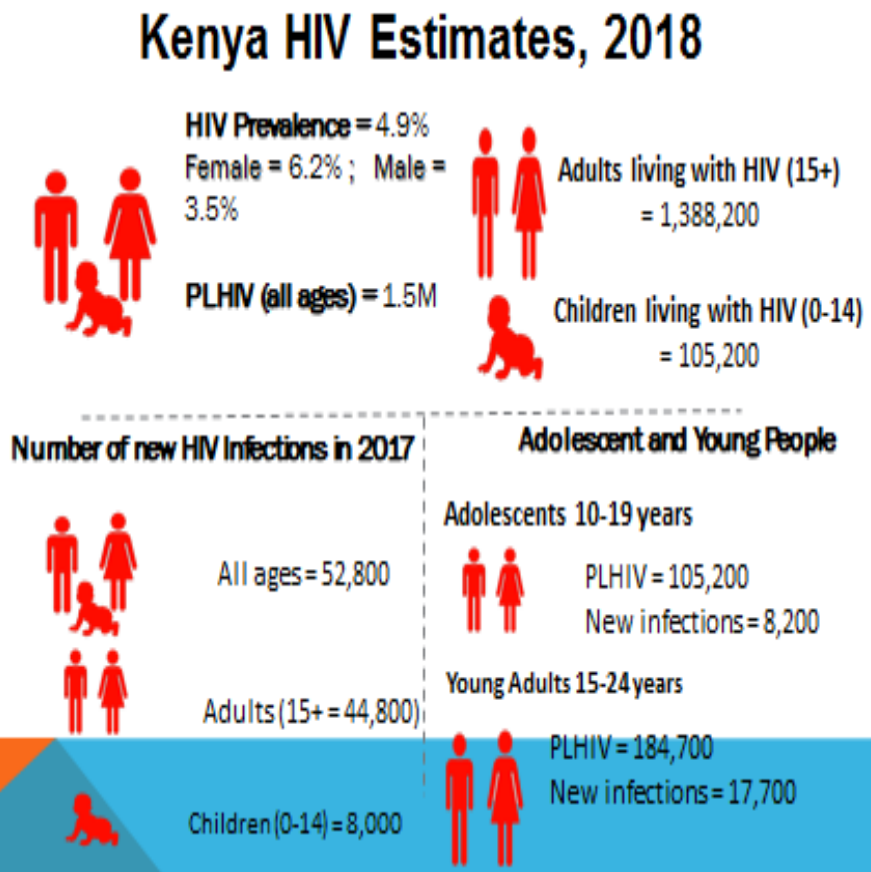
By Douglas Onyancha

KENYA MEDICAL SUPPLIES AUTHORITY — YOUR PARTNER IN HEALTHCARE

KEMSA's integrated supply chain system is tailored to offer the highest quality medical products aimed at:

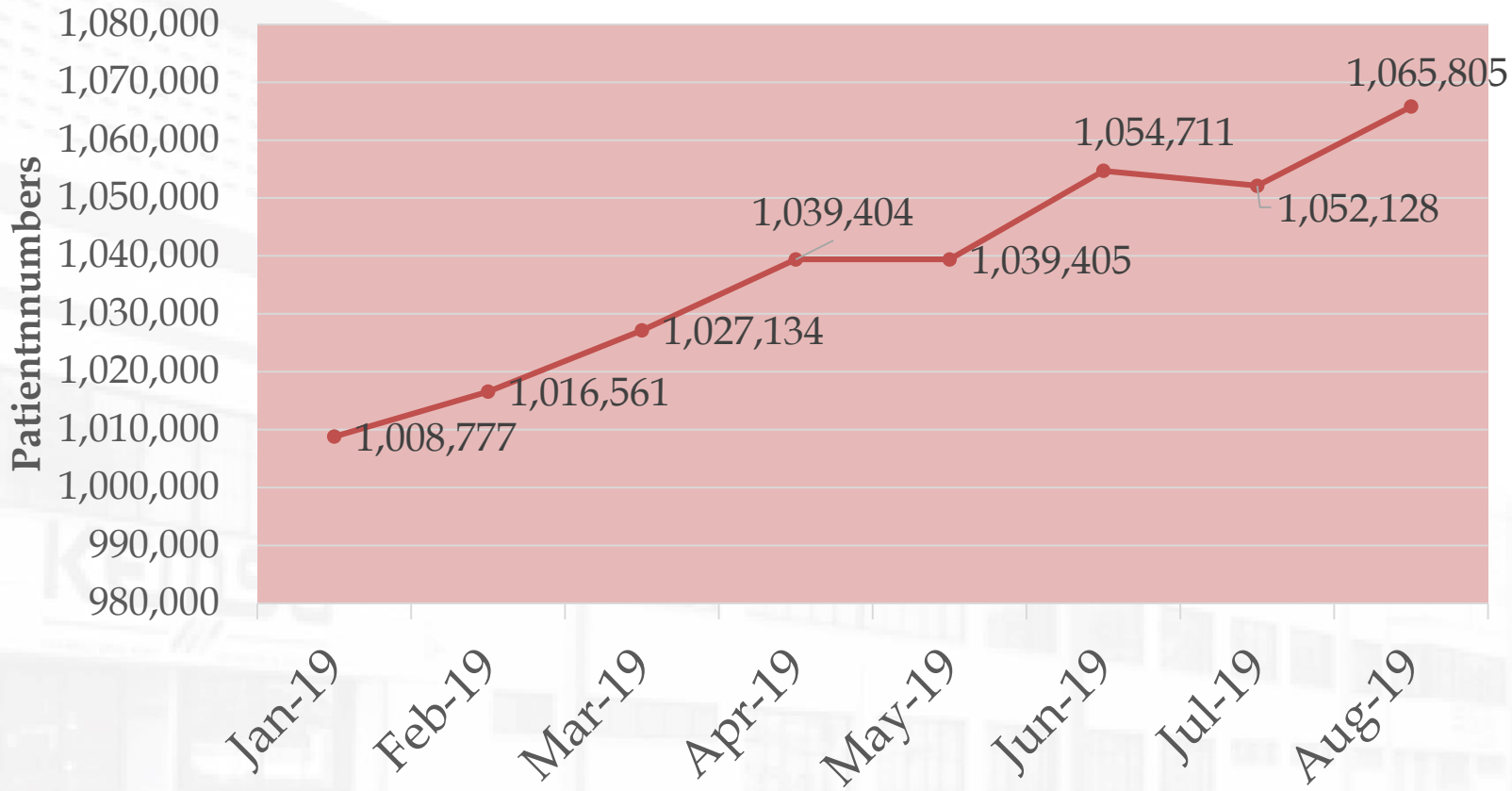
- Lower cost of healthcare
- Increase access to healthcare
- Improve national/County healthcare outcomes

COUNTRY HIV/AIDS LANDSCAPE



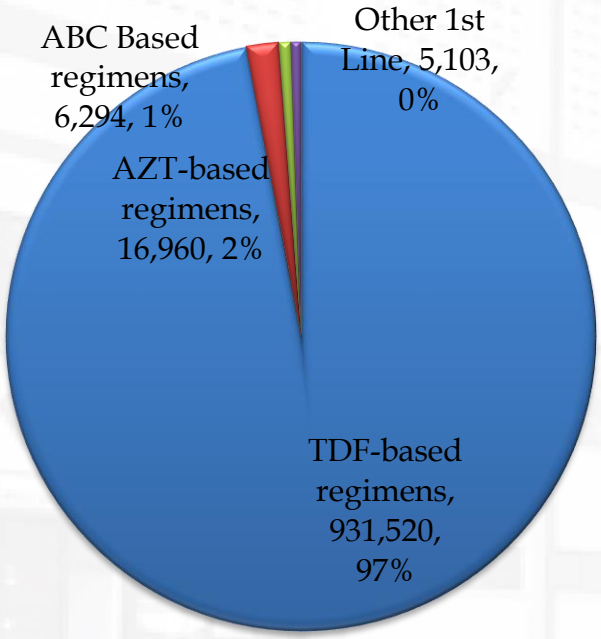
New estimates expected before end of year after release of KENPHIA Results

Patient Scale up

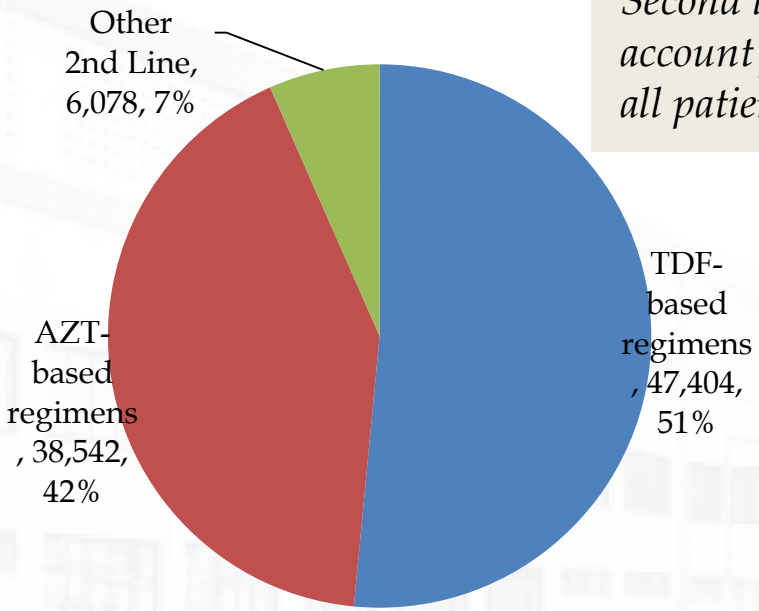


Trends: National ART Regimens

NATIONAL HIGHLIGHTS: Patients are being switched off sub-optimal regimens onto preferred lines of treatment



Key 1st Line Regimens



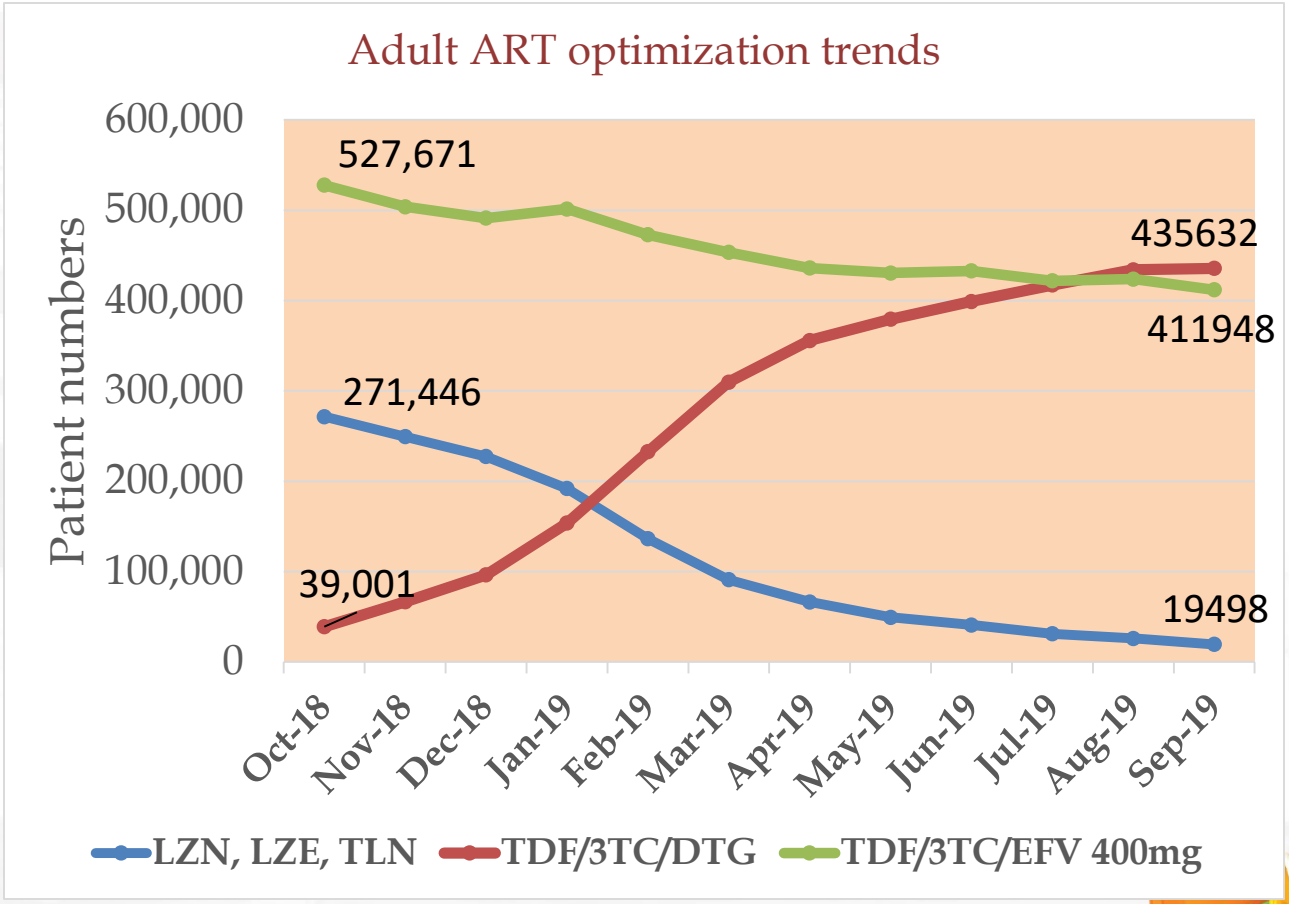
Key 2nd Line Regimens

Second line patients account for 9.31% of all patients on ART

Adult ART Optimization

- Projected split by June 2020
  - TLD: 592,700
  - TLE: 430,428

50% of these patients will be on Multi-month pack of 90s



Paediatric ART Optimization

Paediatrics are being phased out of Nevirapine Based Regimens

Age/Weight	Preferred Regimen
Birth – 4 weeks	AZT + 3TC + RAL1
< 20 kg (above 4 weeks old)	ABC[2] + 3TC + LPV/r
20 kg – 35 kg	ABC[2] + 3TC + DTG
> 35 kg	TDF[2] + 3TC + DTG

Procurement

Procurement process is dependent of funding mechanism:

GoK

- Conducted in accordance to the Kenya Public Procurement and Disposal Act (PPDA)

Global Fund

- Principal Recipient is the National Treasury with obligations set out in the grant agreement and the Procurement and Supply chain Management (PSM) guide
- Procurement conducted in accordance to the Kenya PPDA

PEPFAR

- Procurement done through KEMSA Medical Commodities Programme (KEMSA MCP)
- Procurement conducted in accordance to USAID Federal Acquisition Regulations (FAR) and ADS 312

Key Procurement Milestones

- Annual country ARVs supplier conference
- Single procurement for annual requirements
- Introduction of penalties for late supplies based on LPO value
- Regular supply management reviews-face to face or conference calls

ARVs Budget Trends

FY	16/17	17/18	18/19	19/20
GOK-Counterpart Funding	$8,536,000	$7,024,082	6,225,000	$9,986,600.
Global Fund	$62,561,128	$55,423,864	$ 17,759,635	$ 59,933,828
PEPFAR	$92,000,000	$78,301,486	63,798,699	$44,542,916

Supply Challenges

- Failure to meet contractual delivery lead times
- Delays in providing requisite documents used for application of IDF, Import permit and Tax exemptions
- Delays in providing acceptance letters and Performance Bonds required to facilitate contract signing
- Misalignment of Supplier Sales and Operations teams

Supplier Performance and Risk Management

- Split of awards-ratio dependent on past performance, price and risk.
- Supplier appraisal tool in place
- Weekly penalties for delayed deliveries
- Performing firms to gain in splits of awards

Operating Environment

- Lengthy tax exemption process
- Pre-shipment inspection requirement for pharmaceuticals (temporary suspended for 90 days)

KEMSA

KENYA MEDICAL SUPPLIES AUTHORITY

YOUR PARTNER IN HEALTHCARE

Thank You

Your Partner in HealthCare

www.kemsa.co.ke

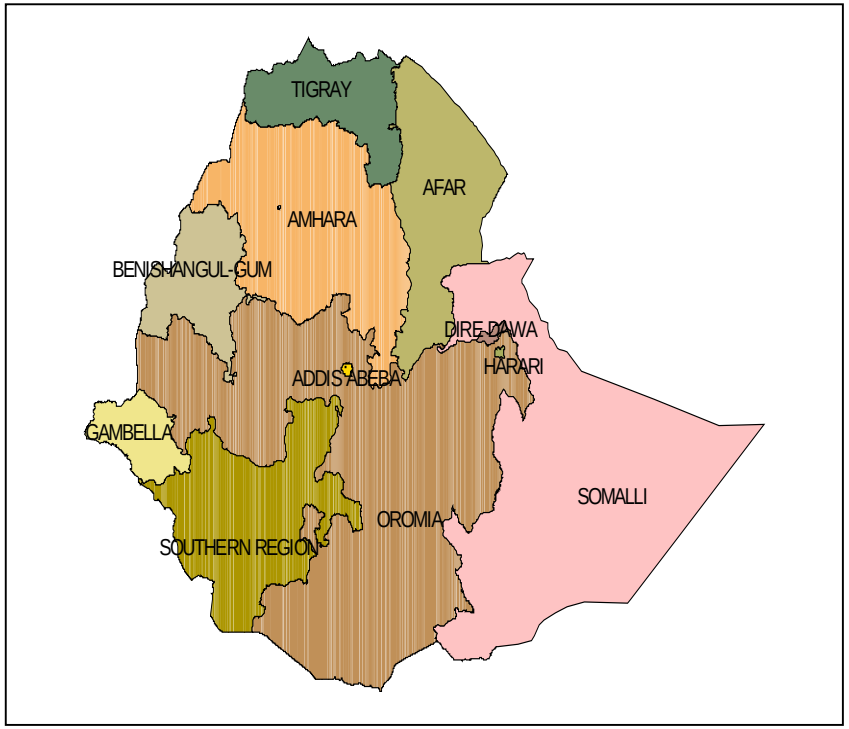
Email: info@kemsa.co.ke, sales@kemsa.co.ke kemsakenya @Kemsa_Kenya

Ethiopia's update on HIV program and procurement

Washington DC

The Mayflower Hotel

November 24-27, 2019

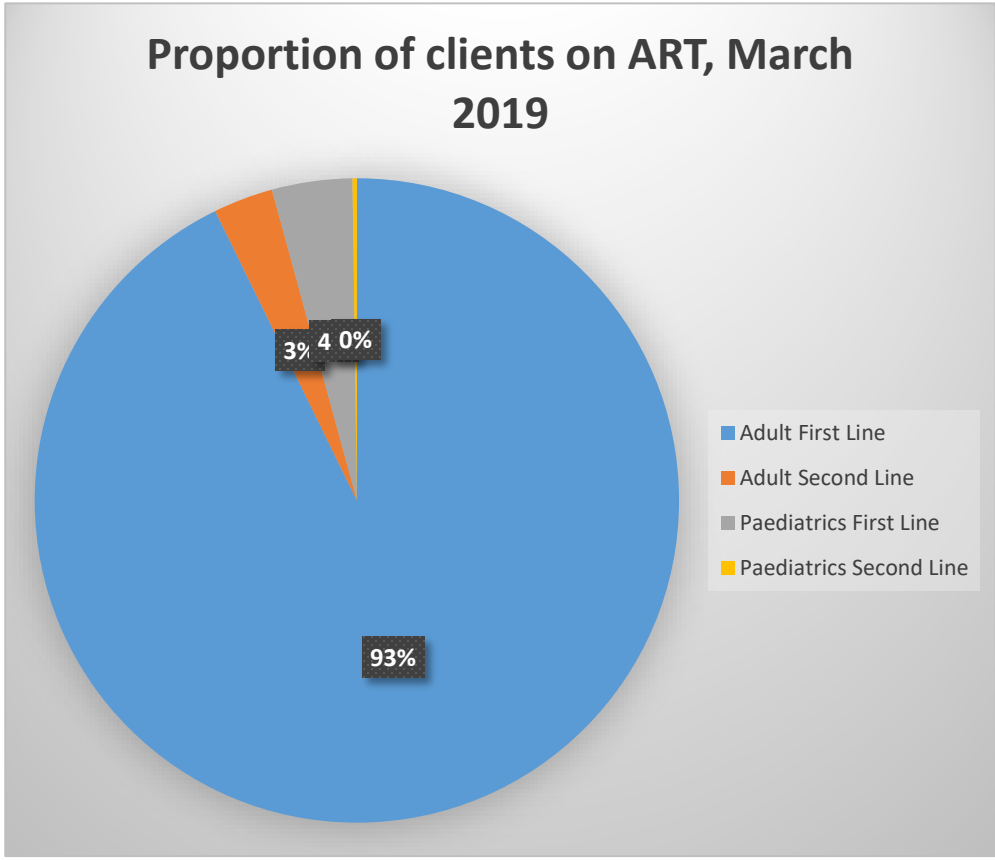


- Ethiopia is a Federal State having nine regional states and two City Administrations
- In 2017, total projected population: 94,351,001 **(CSA 2017)**

- HIV prevalence - 0.9% ,(EDHS 2016)

According to 2019 Spectrum Estimate

- There are an estimated of 698,600 PLHIV in 2019
  - ✓ 34,000 are children under 15 years of age
- Annual New infections estimate in 2019 - 21,486
- Annual AIDS related deaths in 2018 - 11,423
- Currently, 79% of the total PLHIV know their HIV status & 470,000 (67.3%) PLHIV are on Antiretroviral Treatment



Treatment updates in HIV Program

NVP phase out for adult and pediatrics, Pediatrics treatment optimization

- **TLD** – Preferred for adults and adolescents
- TLE – For women of childbearing age, planning to conceive or not using contraceptive
- ABC/3TC/LPV/r – children <10 years and <20kg
- ABC/3TC/DTG - children <10 years and >20kg

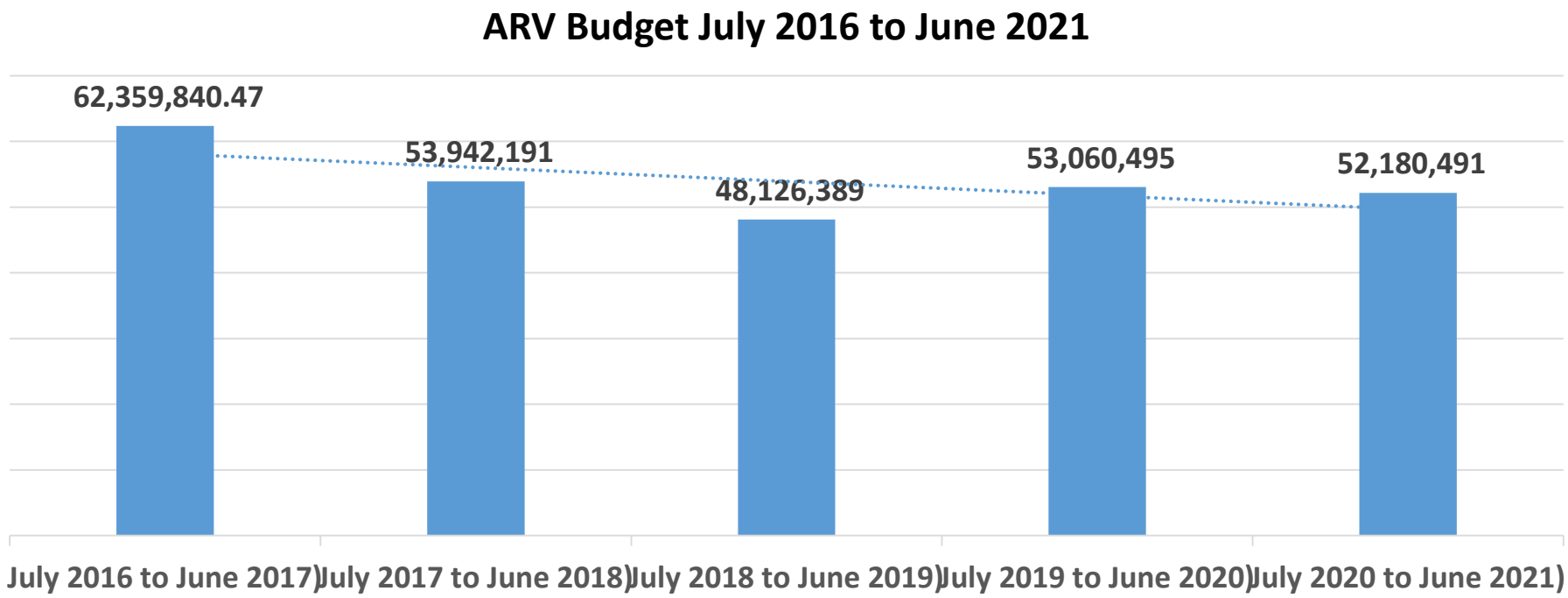
3rd line treatment started at selected hospitals

- Darunavir (DRV) - 600mg – Tablet
- Darunavir (DRV) - 75mg – Tablet
- Dolutegravir (DTG) - 50mg – Tablet
- Ritonavir (RTV) - 100mg – Tablet
- Raltegravir (RAL) 100mg –Tablet
- Ritonavir (RTV) - 25mg – Tablet

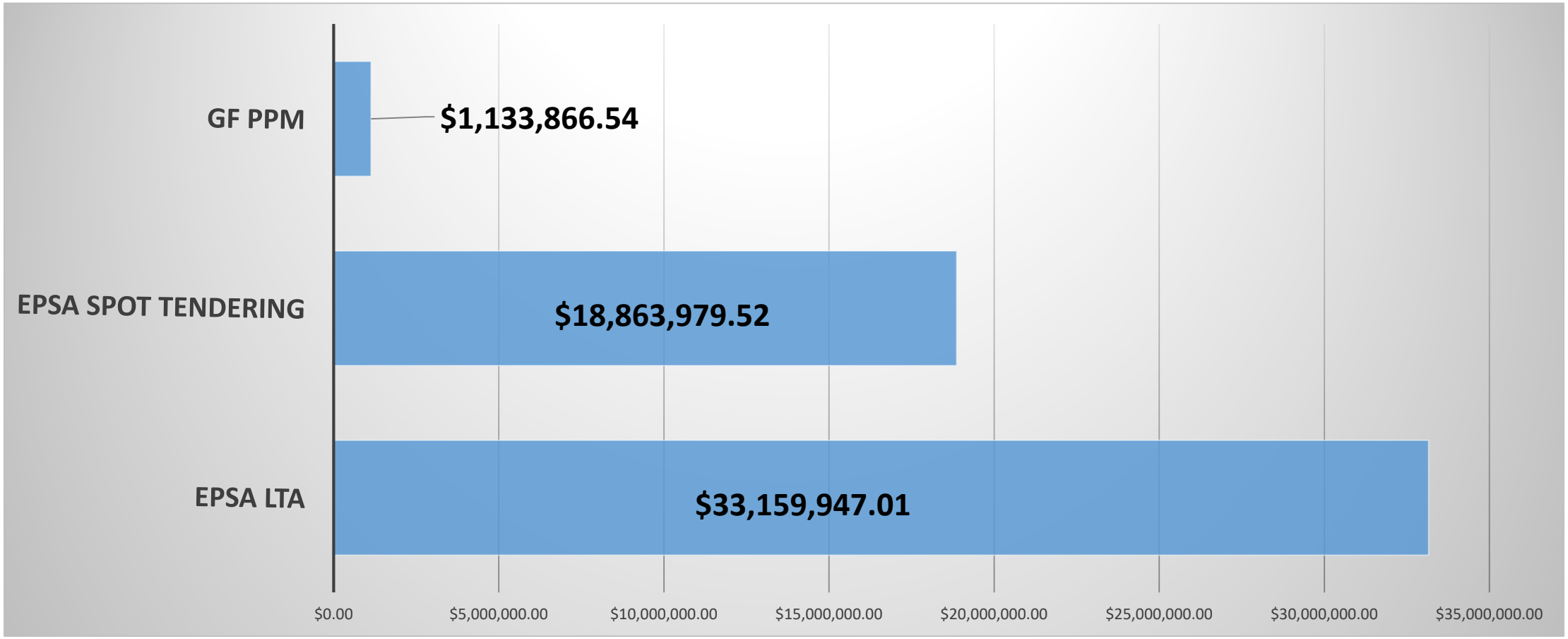
Dual AZT and NVP prophylaxis for HIV exposed infants

ARV Spending and Budget

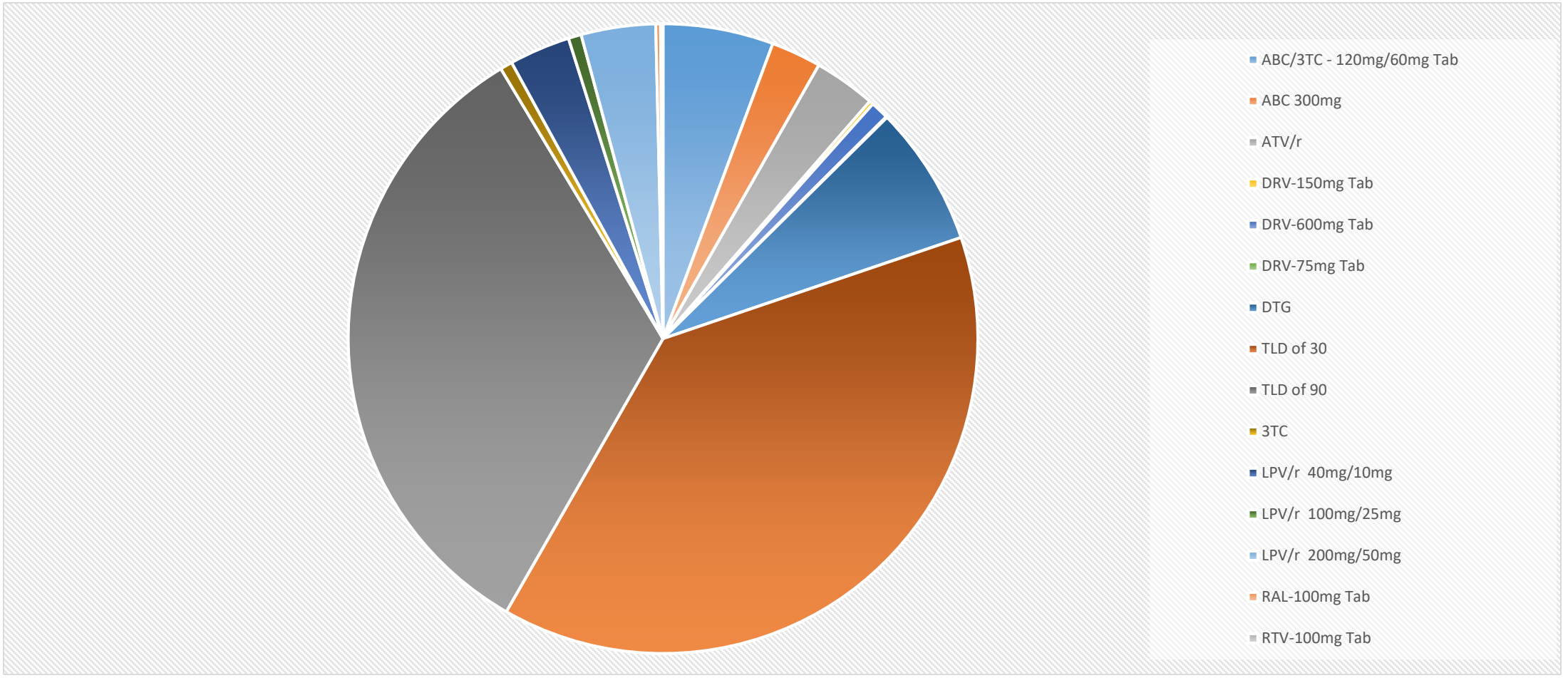
- ARV treatment is provided at 1304 ART sites and 2176 PMTCT sites
- The source of finance is The Global Fund
- The Principal Recipient of the fund is Federal HIV/AIDS Prevention and Control Office-Ethiopia (FHAPCO)
- Procurement is effected by Ethiopian Pharmaceutical Supply Agency (EPSA)
- Commodity forecasting is done annually for 3 consecutive years with one year supply plan.



Current ARVs Procurement for 2019/20



Procurement Expenditure 2019/20



Long term framework agreements

- Eight suppliers have been part of the framework agreement for selected 17 ARVs.50% of allocated quantity
- For most line items award have been shared among two to three bidders by 60% - 25% - 15% or 60% - 40% ratio
- supplier failure and supply shortage risk will be highly minimized because of FW
- After the completion of the first year contract of the FW, EPSA have reviewed the performance of each supplier included and started the second year PO initiation

LTA performance evaluation

Scoring element	Weight
Supplier lead time	50%
Line fill rate	30%
Responsiveness	20%

Performance evaluation scoring

Excellent performance - 90-100%

Very good performance - 80-89%

Good performance - 70-79%

Fair performance - 60-69%

Poor performance <60%

Line fill rate evaluation

No.	Item Description	Quantity	Received QTY	Line Fill Rate%
1	ABC+3TC-120mg+60mg-Tablet	87.646	87.646	100.0%
2	ATV/r-300mg+100mg-Tablet	284.901	284.901	100.0%
3	DRV-600mg-Tablet	6.194	6.194	100.0%
4	DTG-50mg-Tablet	208.062	208.062	100.0%
5	EFV-200mg-Tablet	19.852	19.852	100.0%
6	EFV-50mg-Tablet	29.436	29.436	100.0%
7	TLD	2.200.091	2.200.011	100.0%
8	TDF+3TC-300mg+300mg-Tablet	309.575	309.575	100.0%
9	AZT+3TC-150mg+300mg-Tablet	167.957	101.220	60.3%
10	AZT+3TC-30mg+60mg-Tablet	16.693	16.693	100.0%
11	3TC-150mg-Tablet	18.778	18.778	100.0%
12	LPV/r-200mg+50mg-Tablet	33.213	0	0.0%
13	LPV/r-100mg+25mg-Tablet	9078	9.078	100.0%
14	NVP-10mg/ml-suspension	13622	13.662	100.3%
15	RTV-25mg-Tabiet	5817	0	0.0%
16	RTV-100mg-Tabiet	6194	6.194	100.0%
17	AZT-10mg/ml-solution	92.250	92.250	100.0%
			Average line fill rate	**85.9%**

Lead time evaluation

PO	Item Description	Quantity	L/C/CAD Opening date	Shipped Quantity	Date of shipment	Lead time (Days)	Average Lead time (Days)
a	ATV/r-300mg+100mg-Tablet	113,960	19-Feb-19	113,960	30-Mar-19	39	**39**
b	3TC-150mg-Tablet	18,778	30-Jan-19	8,771	15-Feb-19	54	**72**
				10,007	25-Mar-19	54	
	AZT+3TC-30mg+60mg-Tablet	16,693		14,620	15-Feb-19	16	
				2,073	22-Apr-19	82	
	AZT+3TC-150mg+300mg-Tablet	100,774		34,037	15-Feb-19	181	
c	EFV-200mg-Tablet	19,852	31-Jan-19	19,852	5-Apr-19	64	
	EFV-50mg-Tablet	29,436		7,500	5-Feb-19	64	
				21,936	5-Apr-19	64	
d	TDF+3TC-300mg+300mg-Tablet	123,830	22-May-19	123,830	18-Jul-19	57	**82**
	AZT+3TC-150mg+300mg-Tablet	41,989		41,989	4-Jul-19	43	
e	DRV-600mg-Tablet	6,194	31-Jan-19	2,050	25-Mar-19	53	
	DTG-50mg-Tablet	22,396		4,144	22-May-19	111	
				22,396	4-Jun-19	124	
f	DTG-50mg-Tablet	185,666	23-May-19	28,112	16-Aug-19	85	
				34,310	18-Jul-19	56	
				49,628	27-Sep-19	127	
				73,616	5-Oct-19	135	
g	TLD	20,055	31-Jan-19	19,980	2-Mar-19	33	**85**
	LPV/r-200mg+50mg-Tablet	33,213		-	**Still not shipped**	**181**	
h	TLD	1,300,000	30-Jan-19	769,950	18-Mar-19	47	
				530,045	18-Apr-19	78	

Lead time…

PO	Item Description	Quantity	L/C/CAD Opening date	Shipped Quantity	Date of shipment	Lead time (Days)	Average Lead time (Days)
i	ATV/r-300mg+100mg-Tablet	79,458	25-Jan-19	79,458	2-Feb-19	8	49.5
j	abacavir-300mg- tablet	52,370	22-May-19	26,185	1-Jul-19	40	
				26,185	11-Aug-19	81	
	ATV/r-300mg+100mg-Tablet	91,483		45,742	6-Jul-19	45	
				45,741	11-Aug-19	81	
	TLD	880,036		210,392	11-Aug-19	81	
				203,598	27-Jun-19	36	
				167,710	30-Jun-19	39	
				298,336	6-Jul-19	45	
	TDF+3TC-300mg+300mg-Tablet	185,745		185,745	14-Jun-19	23	
	AZT+3TC-150mg+300mg-Tablet	25,194		25,194	29-Jun-19	38	
	LPV/r-100mg+25mg-Tablet	9078		9,078	7-Aug-19	77	
k	ABC+3TC-120mg+60mg-Tablet	35,276	30-Jan-19	35,276	6/29/2019	150	160
	NVP-10mg/ml-suspension	13,622		13,662	6/29/2019	150	
	RTV-25mg-Tablet	5,817		-	**Still Not shipped**	**181**	
l	AZT-10mg/ml-solution	50,000	25-Mar-19	50,000	30-May-19	66	67.5
m	AZT-10mg/ml-solution	42,250	4-Jul-19	42,250	11-Sep-19	69	
n	RTV-100mg-Tabiet	6194	30-Mar-19	6,194	7-Jun-19	69	69
						Total average lead time	78

Quality, shelf life, and package integrity

Challenges

- Global API manufacturers shrinkage, this creates a problem in fund liquidation and delivery
- Delays in approval of new molecules
- Few qualified manufacturers for some ARVs – supply constraint
- Unwillingness to supply non economic quantities
- Late notification of delays in delivery by some supplies
- Accelerated regimen changes

Strengths

- Strong collaboration among in country stakeholders working on HIV program & in country system improvements
- Good responsiveness of most suppliers
- Improved contract management
- Good support from GF

Thank you!!!

ARV Large Buyer Seller Summit

Republic of South Africa

Ms Khadija Jamaloodien
Affordable Medicines Directorate

ARV Large Buyer Seller Summit
November 2019
Day 1

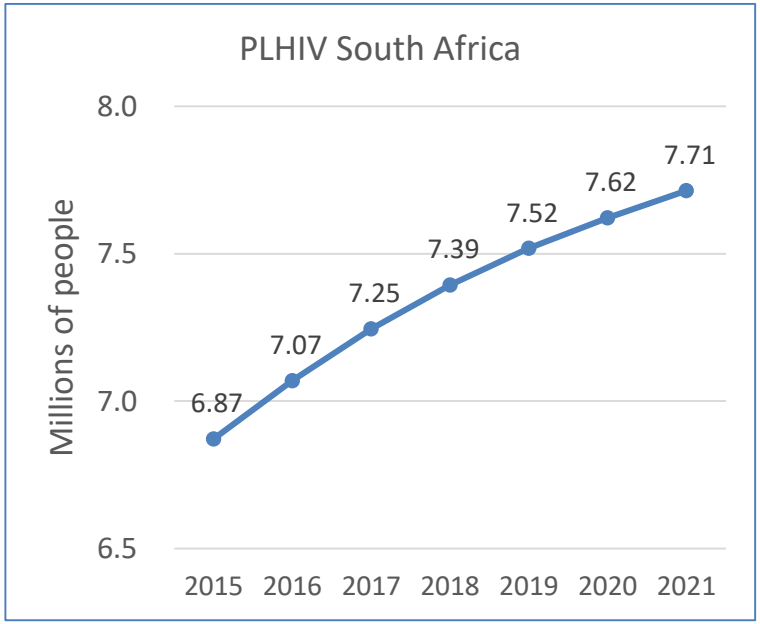
health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

Contents

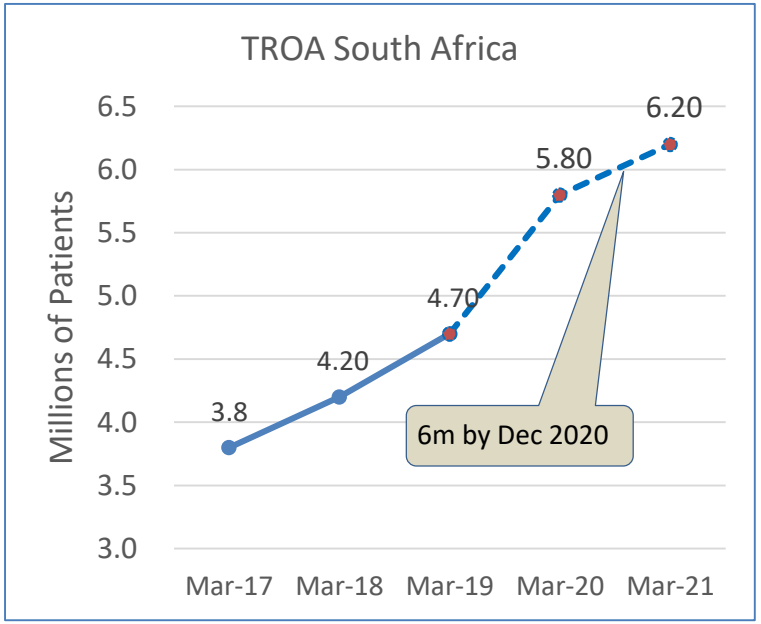
HIV & AIDS in South Africa

People living with HIV (PLHIV) is growing, but at a slower rate



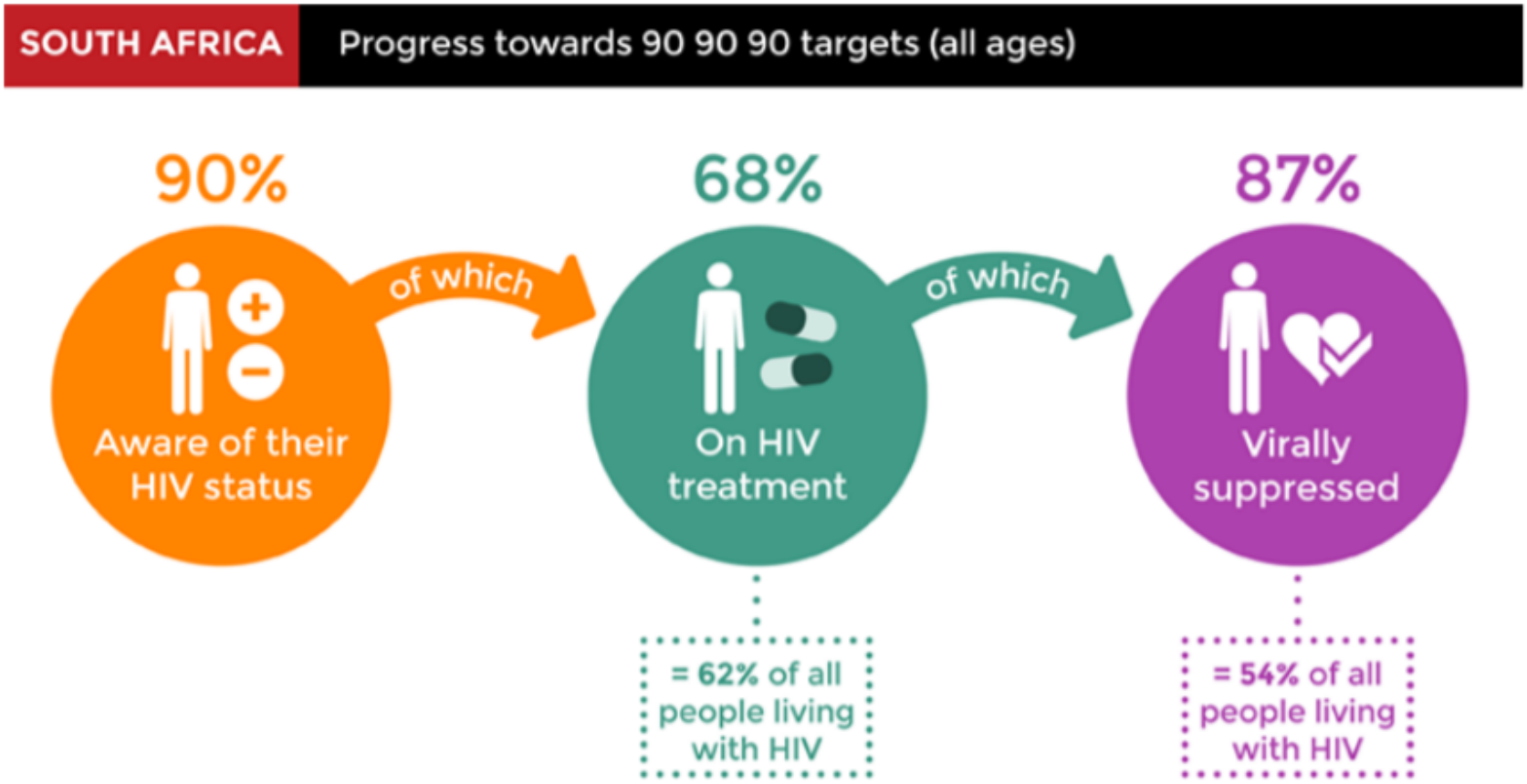
Source
- Thembisa 4.2 model

Department of Health has set aggressive growth targets for this year



Source
- NDoH

Progress towards 90-90-90



*Viral suppression based on <400 copies/ml; next iteration of guidelines will reduce this to <50 copies/ml where suppression rates are ~50%

Contents

NDoH selection and procurement processes

National roll-out of new medications requires inclusion in formal NDoH selection and procurement processes

- ARV Procurement Committee:
  - Experts in adult and paediatric HIV care were consulted to agree with the proposed new regimens
- Formal process through Essential Drugs Programme (EDP), National Essential Medicines List Committee and relevant HIV clinical committees underway for the review of the National Treatment Guidelines

New product introductions are informed by regulatory landscape and security of supply

Timing of procurement dependent on adequate number of suppliers receiving regulatory approval

- Continuous regulatory landscape analysis
- Collaboration with applicants and SAHPRA

Security of supply imperative for all products procured on national tender

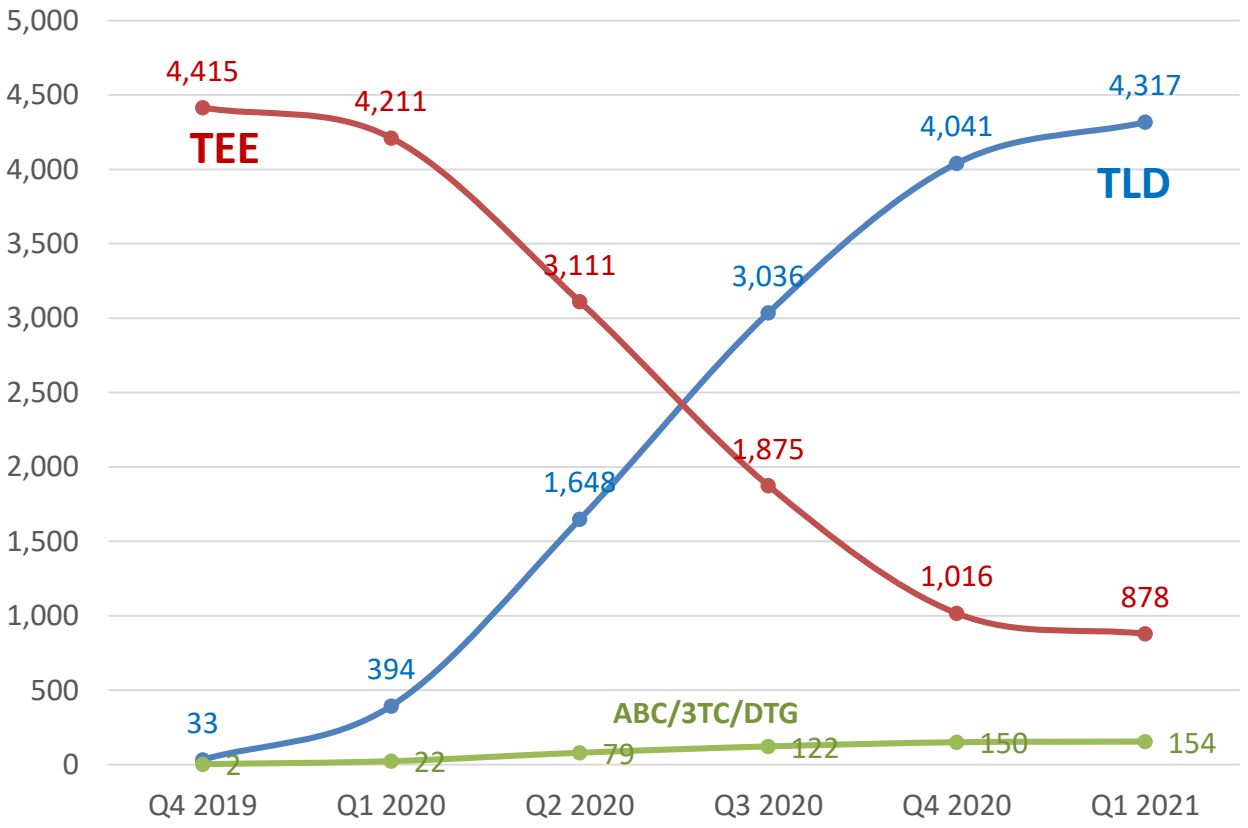
- Sufficient production capacity
- Diversification of supply inputs

Status update: ARV Supplementary tender

- Supplementary tender driven by updated estimates vs original tender
  - Additional TEE required due to delay in transition to TLD
  - Additional TE required for PrEP
  - Revised estimates for some other ARVs as well
- Expected timing
  - Bid adjudication completed
  - Discussions with suppliers to follow
  - Expected date for award announcement is mid-December

Contents

Adults on 1st line ART



Source: Team analysis; TEE/TLD profile based on input from provinces together with modelling of qualifying patients

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

Regimen split: 2nd line adults

	Dec-19	Dec-20	Dec-21	Comment
AZT/3TC+LPV/r	275,779	257,807	246,169	In adult 2L, LPV/r will continue for existing patients and DTG 50 introduced for current 1L patients failing on treatment
AZT/3TC+DTG	8,253	68,071	79,776	
AZT/3TC+ATV/r	10,658	9,963	9,314	Stable volumes expected
TDF/FTC+LPV/r	5,993	5,603	5,237	
TDF/FTC+ATV/r	242	226	211	
Total	**300,924**	**341,670**	**340,708**	

Source: Team analysis; based on latest ARV guidelines (awaiting sign-off)

Regimen split: 1st line children

	Dec-19	Dec-20	Dec-21	Comment
ABC/3TC+EFV	92,889	↘ 17,058	16,563	Expectation that EFV & LPV/r will be replaced by DTG 50
ABC/3TC+LPV/r	46,621	↘ 7,697	6,604	
ABC/3TC+DTG	1,710	↗ 129,031	139,691	
AZT/3TC+NVP	6,338	6,371	6,403	
ABC/3TC+ATV/r	3,375	945	1,244	
Total	**150,933**	**161,102**	**170,504**	

AZT/3TC/NVP

Contents

Status of TLD transition

Official launch by Minister planned for 27 November 2019

- Training to ensure at least 1 clinician per site trained prior to launch
- Communications plan driven by HIV Programme
- Frequent interaction between suppliers and TLD planning team
- Expect slow uptake over SA's Dec/Jan holiday
- Will accelerate from Feb 2020 onwards

National demand plan

Calendar period	**Q4 - 2019**	**Q1 - 2020**	**Q2 - 2020**	**Q3 - 2020**	**Q4 - 2020**
'000s of packs					
Opening stock DoH	293	1 013	4 525	8 724	11 827
Issues to Patient	78	1 393	5 834	10 747	14 305
Expected order placement	798	4 906	10 032	13 850	15 179
Closing stock DoH	1 103	4 525	8 724	11 827	12 701

Note: Stock levels based on 2.5 months of cover; orders calculated to achieve stock level target
Source: based on demand plans as at 8 November; subject to change as provinces confirm their individual launch dates

TLD Supply plan

Calendar period	**Q4 - 2019**	**Q1 - 2020**	**Q2 - 2020**	**Q3 - 2020**	**Q4 - 2020**
'000s of packs					
Supplier Opening Stock	1 868	2 689	6 210	8 928	10 050
Estimated orders from DoH	846	4 871	10 032	13 850	15 179
Production/Imports	1 667	8 393	12 751	14 971	15 317
Closing Stock	2 689	6 210	8 928	10 050	10 188
Surplus/Shortfall to stock target*	198 390	0	0	0	0

*Surplus stock due to delayed start and stock already at suppliers
Note: Stock levels based on 2 months of cover; production/imports calculated to achieve stock level target
Source: based on demand plans as at 8 November; subject to change as provinces confirm their individual launch dates

THANK YOU

UNDP Procurement Update
25 November 2019

UNDP Global Fund / Health Implementation Support Team

Zafar Yuldashev, Procurement Specialist

UNDP AT A GLANCE

A strategic practice that contributes to effective program delivery.

170+ The number of countries and territories where UNDP is working on the ground

3 Primary Focus Areas:

- Sustainable development
- Democratic governance and peacebuilding
- Climate and disaster resilience

PROCUREMENT TREND (MILLION USD)

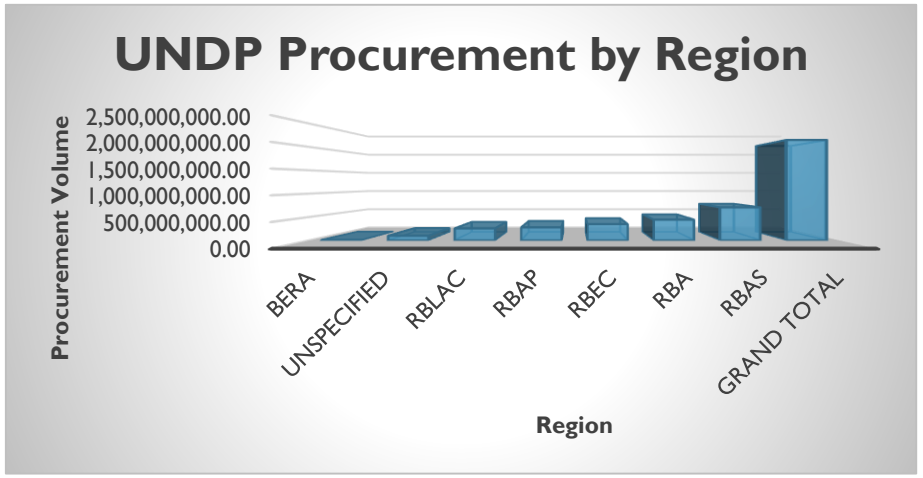
The UNDP procurement function is implemented through a decentralized business model across all Country Offices

IN 2018, UNDP'S PROCUREMENT VOLUME WAS

$2,146,494,997.62

11.37% of total UN Procurement

Services account for 70%



UNDP GF HIST Mission

UNDP's Mission: Eradicate poverty, reduce inequalities and exclusion, strengthen effective and inclusive governance, and build resilient and sustainable systems for health.

In line with Sustainable Development Goals including SDG 3, UNDP Strategic Plan & UNDP HIV, Health & Development Strategy 2016–2021

"UNDP health procurement and supply management is a development activity and inseparable from the strengthening of national capacities for equitable and sustainable delivery of essential health services." November 2017

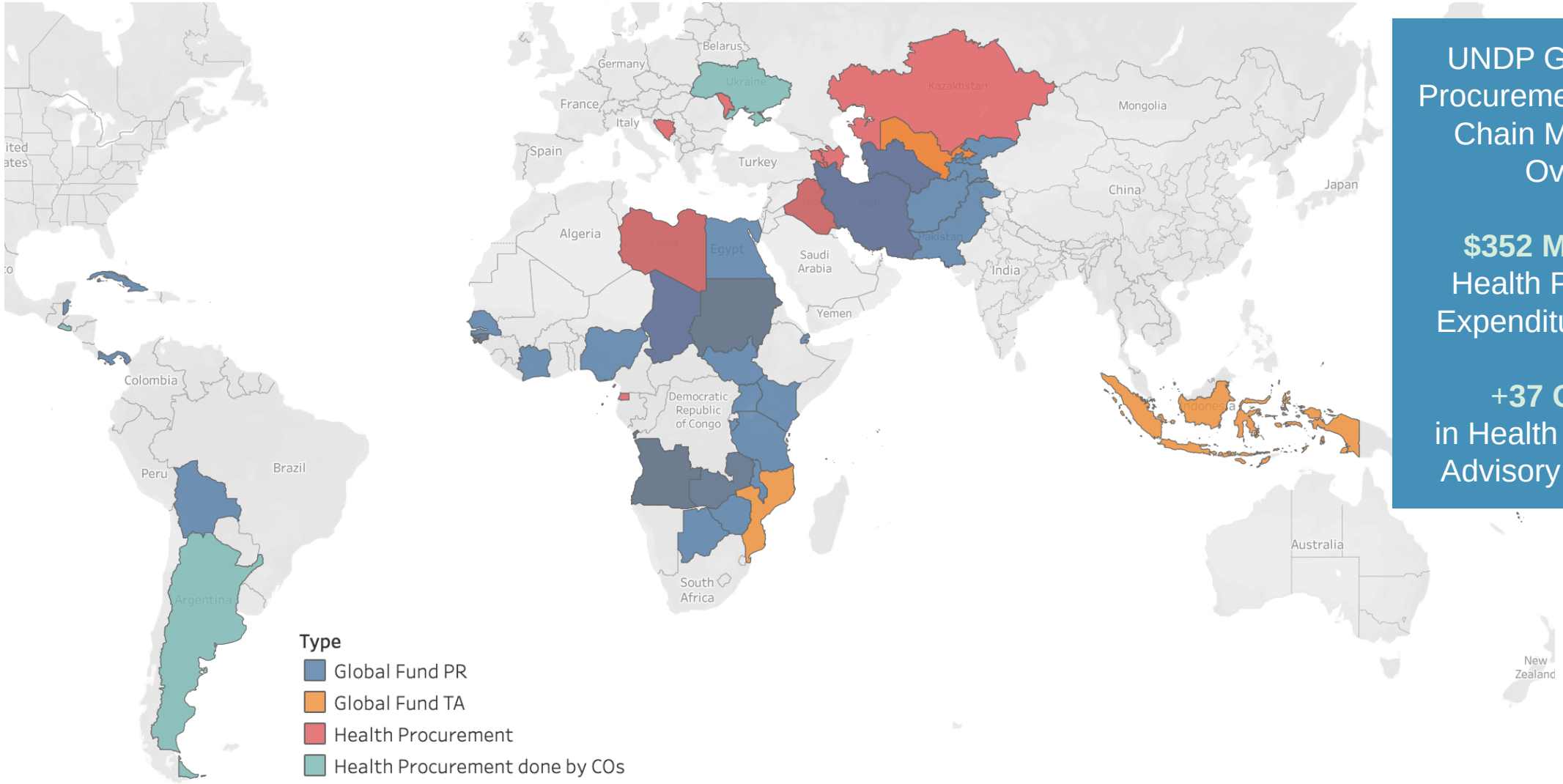
Since 2003, the **UNDP Global Fund/ Health Implementation Support Team (GF-HIST) in collaboration with Country Offices** provides **specialized advisory** and **health procurement** support in some of the most challenging operating environments to ensure the quality and reach of essential health services and to improve peoples' lives.

Currently totaling **US$1.366 billion** in signed agreements

≈ **352 M$ Health Procurement** in 2018 with more than **50% for NCDs medicines**

For more information on our work, please refer to the GF/HIST Annual Report 2016-2017

Portfolio overview



UNDP Global Health Procurement and Supply Chain Management Overview

$352 Million USD
Health Procurement Expenditure Delivered

+37 Countries
in Health Procurement Advisory and Support

UNDP PROCUREMENT ARCHITECTURE

A large variety of health products is procured by UNDP globally:

- Medicines (HIV, TB, NCDs, e.g.)
- LLINs & insecticides
- Medical devices including diagnostic kits
- Health equipment
- Laboratory equipment and consumables (reagents, cartridges)

UNDP PROCUREMENT ARCHITECTURE

- **UNDP uses Long Term Agreements (LTAs):**
  - with manufacturers for most frequently procured products (large volumes)
  - with consolidators / wholesalers of health products (IDA, IMRES, Amex, MEG, Svizera…etc)

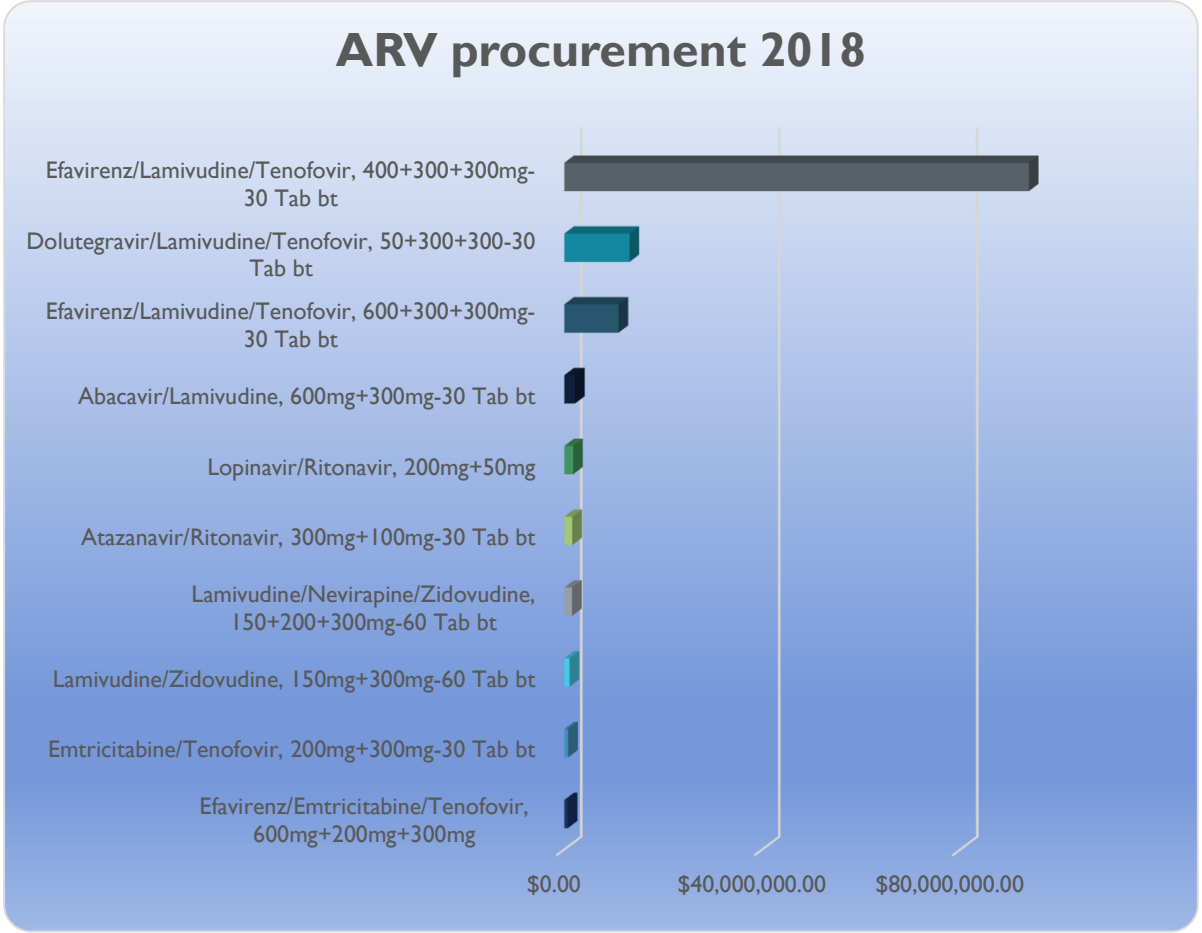
- **Partnerships with sister United Nations agencies specialized for certain types of health products:**
  - UNFPA: condoms, lubricants…etc
  - UNICEF: pediatric ARVs, malaria medicines, LLINs and other essential medicines
  - UNOPS/Stop TB/Global Drug Facility: 2nd line TB medicines, soon 1st line medicines and diagnostics

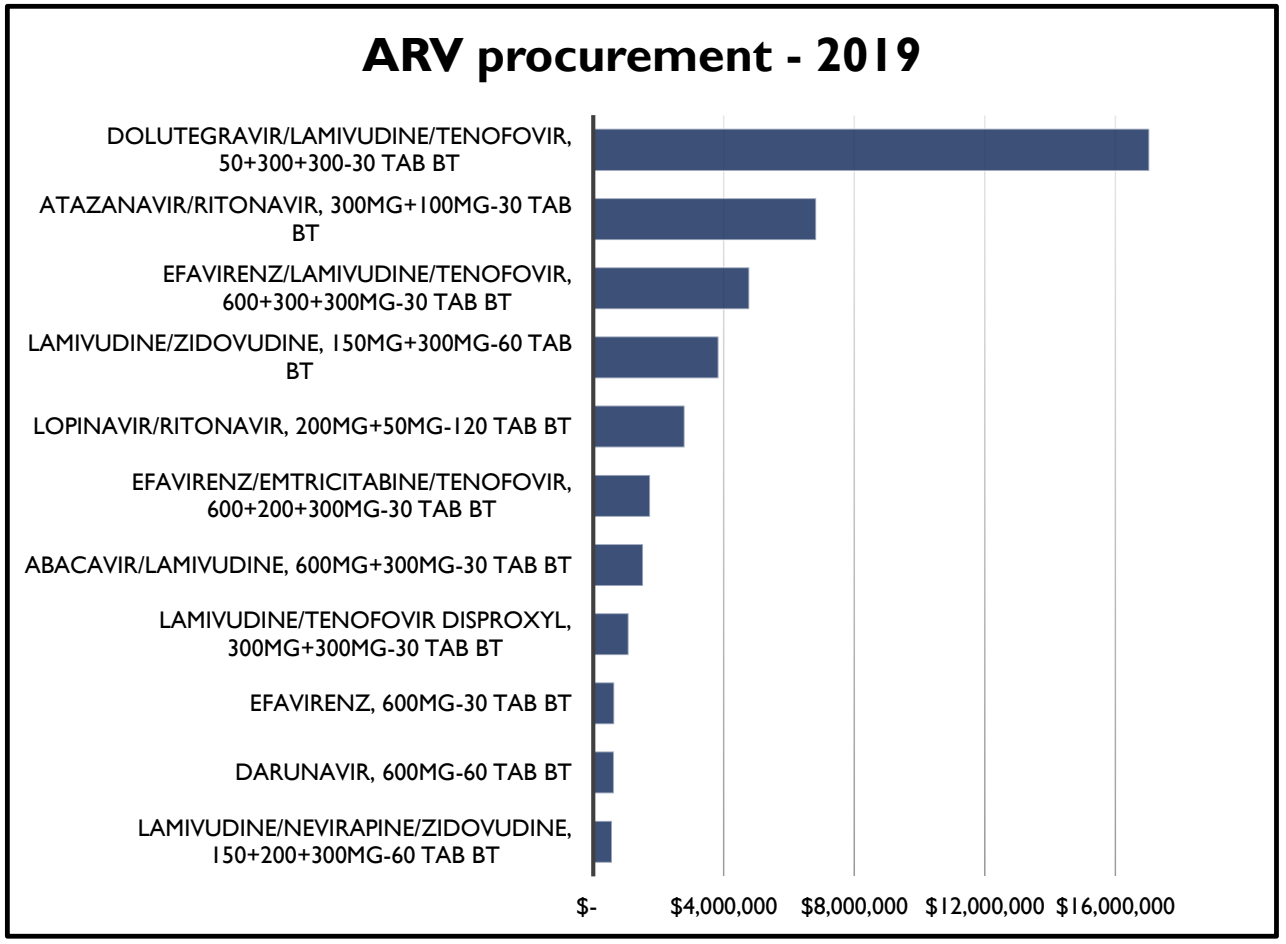
- **International tenders whenever the systems in place do not allow to procure certain products or for big quantities**

Product
Abacavir, 300 mg, 60 Tab Bottle
Abacavir/Lamivudine, 600mg+300mg, 30 Tab Bottle
Atazanavir/Ritonavir, 300mg+100mg, 30 Tab Bottle
Darunavir, 400mg, 60 Tab Bottle
Darunavir, 600mg, 60 Tab Bottle
Efavirenz, 600mg, Blister of 10-30(3*10)
Efavirenz, 600mg, 30 Tab Bottle
Efavirenz/Emtricitabine/Tenofovir, 600mg+200mg+300mg, 30 Tab Bottle
Efavirenz/Lamivudine/Tenofovir, 400mg+300mg+300mg, 30 Tab Bottle
Efavirenz/Lamivudine/Tenofovir, 400mg+300mg+300mg, 90 Tab Bottle
Efavirenz/Lamivudine/Tenofovir, 600mg+300mg+300mg, 90 Tab Bottle
Emtricitabine/Tenofovir, 200mg+300mg, 30 Tab Bottle
Lamivudine/Nevirapine/Zidovudine 150mg+200mg+300mg, 60 Tab Bottle
Lamivudine/Tenofovir Disproxyl 300mg+300mg, 30 Tab Bottle
Lamivudine/Zidovudine 150mg+300mg, 60 Tab Bottle
Lopinavir/Ritonavir, 200mg+50mg, 120 Tab Bottle
Nevirapine, 200mg, 60 Tab Bottle
Ritonavir, 100mg, 30 Tab Bottle
Tenofovir disoproxil, 300mg, 30 Tab Bottle
Zidovudine, 300mg, 60 Tab Bottle
Dolutegravir, 50mg, 30 Tab Bottle
Dolutegravir/Lamivudine/Tenofovir, 50mg+300mg+300mg, 30 Tab Bottle
Dolutegravir/Lamivudine/Tenofovir, 50mg+300mg+300mg, 90 Tab Bottle

LIST OF ADULT ARVS (UNDER LTAS)

ARV VOLUMES (ADULT)





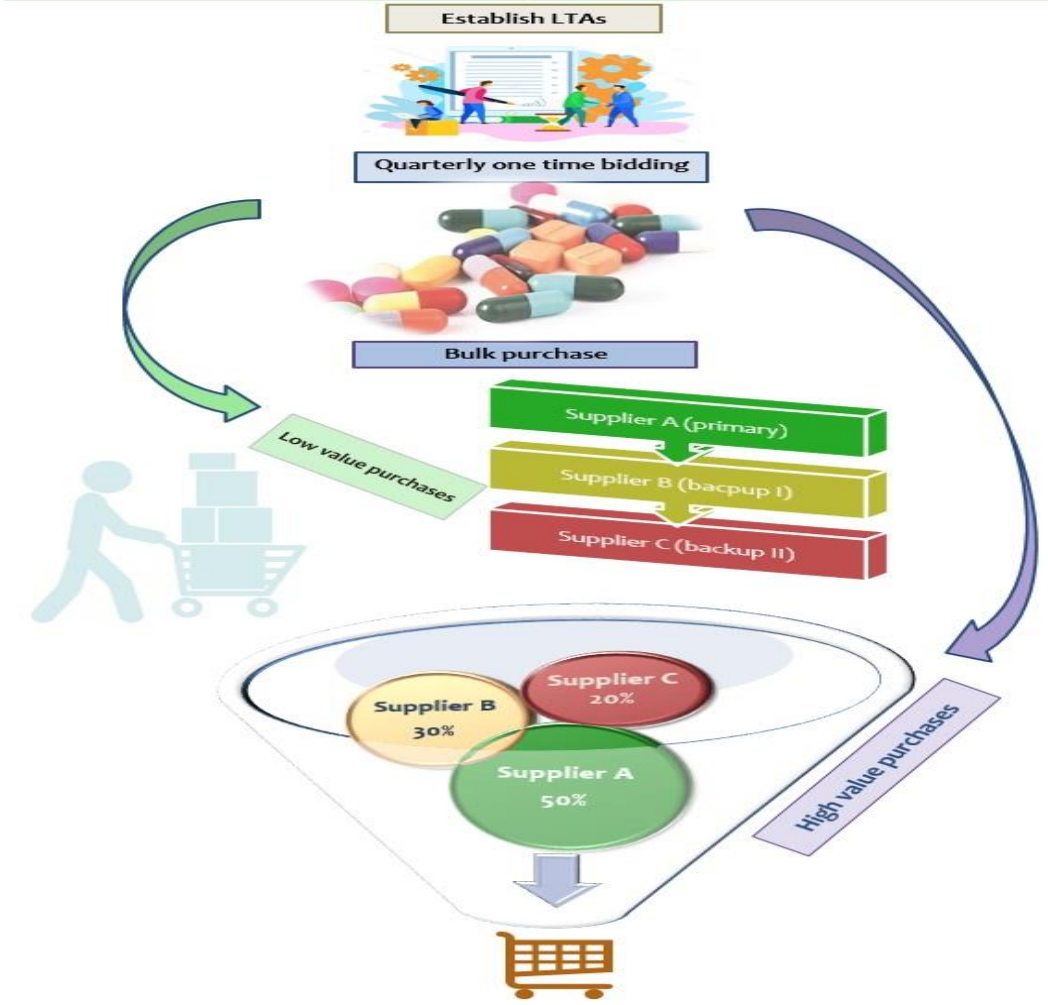
PROJECTION FOR NEW LTAS

Product description	Strength	Dosage form
Abacavir	300 mg	Tablet
Abacavir/Lamivudine	600 mg + 300 mg	Tablet
Abacavir/Dolutegravir/Lamivudine	600 mg + 50 mg + 300mg	Tablet
Atazanavir/Ritonavir	300 mg + 100 mg	Tablet
Darunavir	600 mg	Tablets
Dolutegravir /Lamivudine/Tenofovir disoproxyl fumarate	50mg+300mg+300mg	Tablet
Dolutegravir	50 mg	Tablet
Darunavir/Ritonavir	400 mg + 50 mg	Tablet
Efavirenz	600 mg	Tablet
Efavirenz/Emtricitabine/Tenofovir disoproxyl fumarate	600 mg + 200 mg + 300 mg	Tablet
Efavirenz/Lamivudine/Tenofovir disoproxyl fumarate	400mg+300mg+300mg	Tablets
Efavirenz/Lamivudine/Tenofovir disoproxyl fumarate	600 mg + 300 mg + 300 mg	Tablets
Emtricitabine/Tenofovir disoproxyl fumarate	200 mg + 300 mg	Tablet
Lamivudine	150 mg	Tablet
Lamivudine/Nevirapine/Zidovudine	150 mg + 200 mg + 300 mg	Tablets
Lamivudine/Tenofovir disoproxyl fumarate	300 mg + 300 mg	Tablet
Lamivudine/Zidovudine	150 mg + 300 mg	Tablet
Lopinavir/Ritonavir	200 mg + 50 mg	Tablets (heat stable)
Nevirapine	200 mg	Tablet
Raltegravir	400 mg	Tablet
Ritonavir	100 mg	Tablet
Tenofovir disoproxyl fumarate	300 mg	Tablet

NEW PROCESS TO ESTABLISH LTAS (TENDER WILL BE ANNOUNCED IN DECEMBER)

Current practice

Future practice



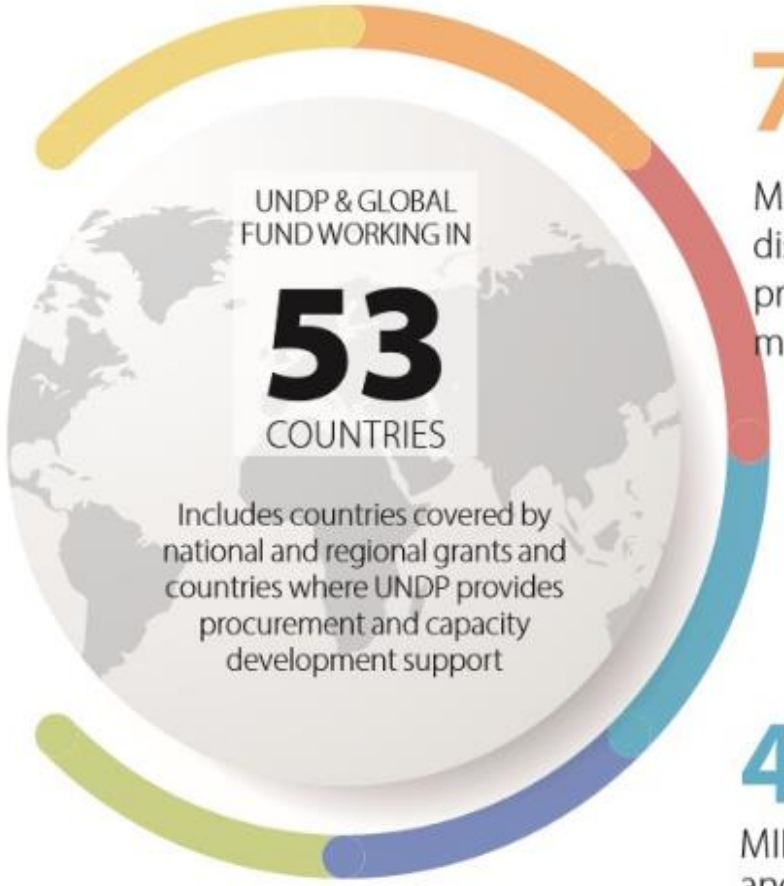
Results supported by UNDP-managed Global Fund grants since 2003

3.1 million LIVES SAVED

Meaning 3.1 million people can live fuller and more productive lives, support their families and contribute to their communities.

19,000 PEOPLE treated for drug-resistant TB

891,000 CASES of TB detected and put on treatment



75 MILLION cases of malaria treated

74 MILLION bed nets distributed to protect families from malaria

1.4 MILLION people receiving HIV treatment

47 MILLION people counselled and tested for HIV

THANK YOU!!!

zafar.yuldashev@undp.org

Global Fund update and priorities. Antiretroviral Large Buyers and Sellers Forum 2019

24 - 27 NOVEMBER 2019

WASHINGTON DC

The Global Fund

Key contacts here today

Martin Auton
Senior Manager, Principal Recipient Services

Uranchimeg Badarch
Strategic Sourcing Category Lead: ARVs

Chirag Rajpuria
Principal Recipient Services

Sunil Garg
Principal Recipient Services

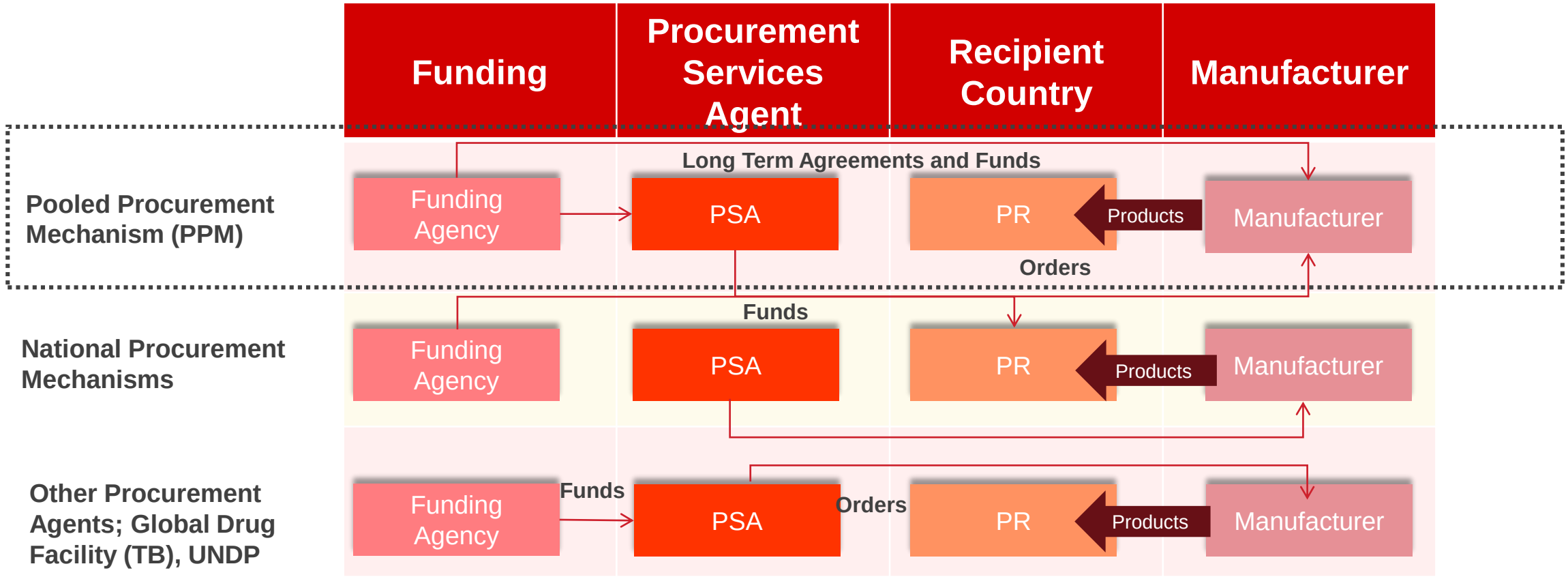
Veronika Zhirnova
Strategic Sourcing

This presentation outlines:

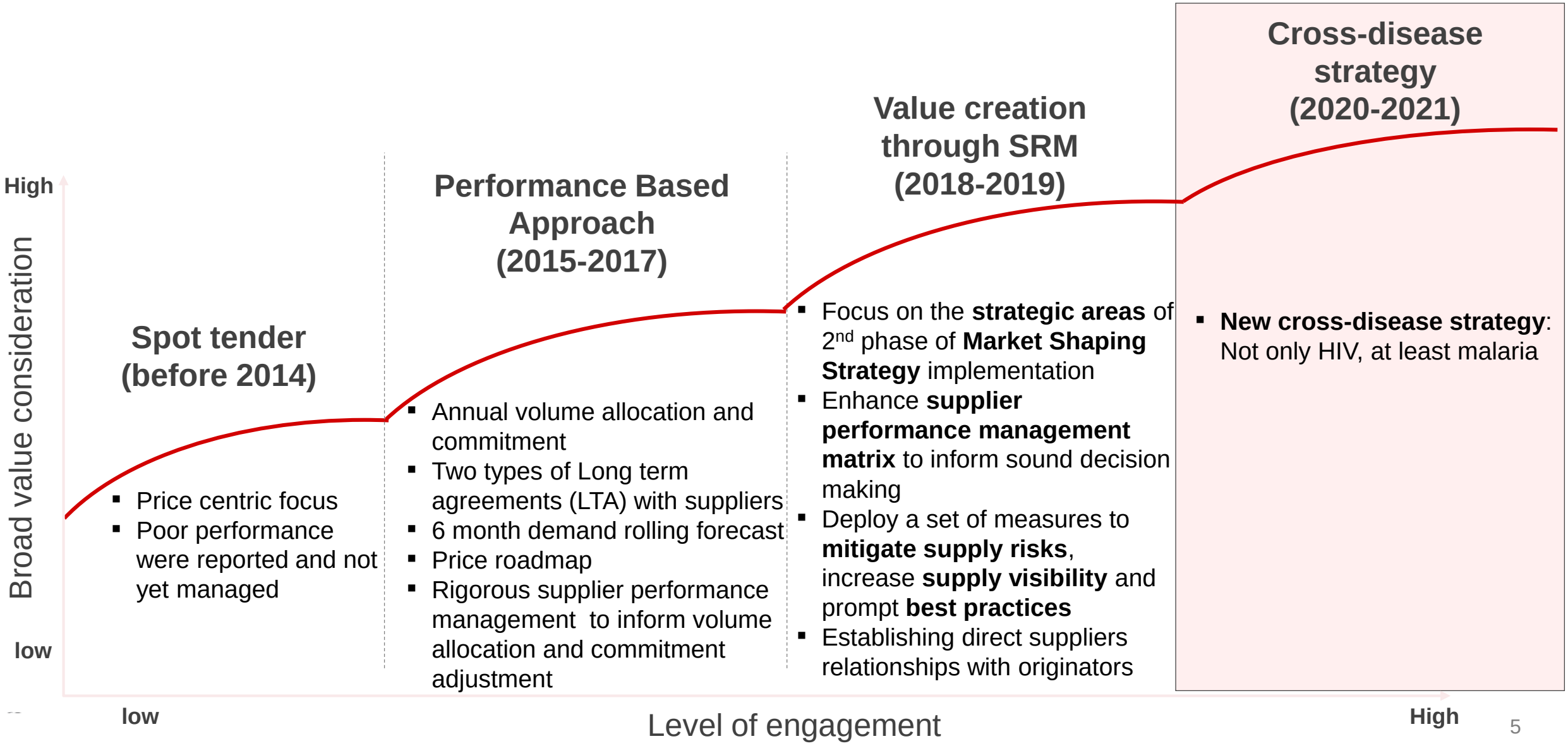
- Implementation of the 2020-2021 Strategy and priorities
- 2019 supplier performance and reporting
- 2020 volumes and allocation
- 2019 key highlights
- Further information

Reminder: Global Fund procurement channels

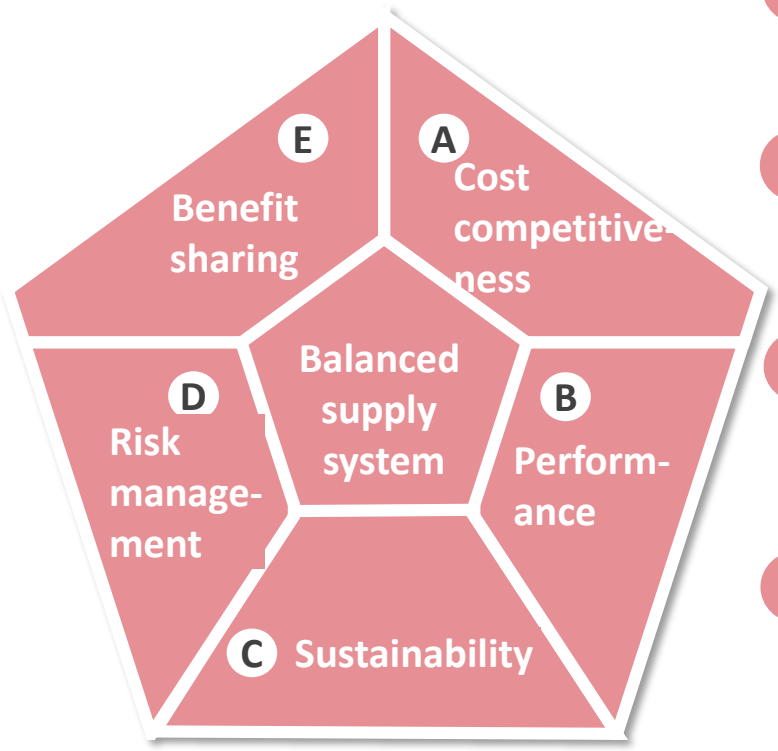
There are a number of procurement channels - with the Pooled Procurement Mechanism representing around 55% total Global Fund health product spend (depending on category)



Evolution of the implementation of ARV strategies with emphasis on value creation through Supplier Relationship Management and cross-disease strategy



Key achievements of 2018-21 ARV procurement strategy, anchored in the balanced supply system of the Global Fund's Market Shaping Strategy, include



A

- Providing **57m monthly packs** per year through PPM **at the lowest possible affordable and sustainable price;** sufficient supply for **4.2m people on treatment**
- An average **16% price reduction for first-line ARV regimen in 2018-2019**

B

- Increase in **OTIF** (on-time-in-full delivery) **to 90%** in 2018-2019 through PPM
- **More responsive supply**: shorter lead-times, VMI and stock visibility for low volume products and stock-outs

C

- **Created a resilient supplier base** to ensure **sufficient supply of all the needed products** and **expanded supplier geographic locations**
- **Accelerated introduction and uptake of new products**
- **90% of first-line ARV products** procured **without secondary carton in 2019** through PPM

D

- **More proactive management of quality** and other **risks**
- **De-risking API/KSM supply**
- Encouraging **participation in WHO collaborative** and **regional pooled registration initiatives**

E

- **Leveraging volumes** and **extending terms to other buyers** through PPM to improve access **to new and/or low volume products** including **non-ARV medicines used in HIV programs**
- **Procurement capability building** with countries (Ethiopia)
- Publishing **reference prices** and **benchmarking**
- **Broader national registration footprints**

Supply chain optimization is one of the key priorities for 2020

- Reduction of request to delivery lead-times by 2-3 months (from 5-6 to 3-4 months)
- Increased frequency of deliveries for 1st line products

We will be having workshops where we want the manufacturers supply chain teams/expertise present

- GS1 standards

- Carton-less packaging

Leveraging impact

PAHO STRATEGIC FUND

The Global Fund

Partnership

Since July 2015, PAHO has been leveraging Global Fund long term agreements (LTAs) for procuring the majority of the ARVs purchased through the Strategic Fund

Added value

- ✓ Vendor performance
- ✓ Supply assurance of products with low volume
- ✓ Access to products allocated to the Global Fund for emergency requests
- ✓ Best value for money

Economy of scale

- ✓ Maximize use of LTAs: framework agreements
- ✓ Increase ARV demand visibility to secure availability
- ✓ Transition/adoption of new products: market intelligence

Effectiveness

- ✓ Contract Supplier Management
- ✓ Harmonize Quality Standards & Quality Assurance
- ✓ Transparency in tendering process (eligibility, technical proposal & evaluation process)

Global Fund and Unitaid work in collaboration and have improved access and/or scaled-up new/better products in 2019

Improved access to **rifapentine**

- In collaboration with Unitaid, leveraging GF long-term agreements and wambo platform, **67% price reduction, from $45 to $15 per treatment,** was achieved.

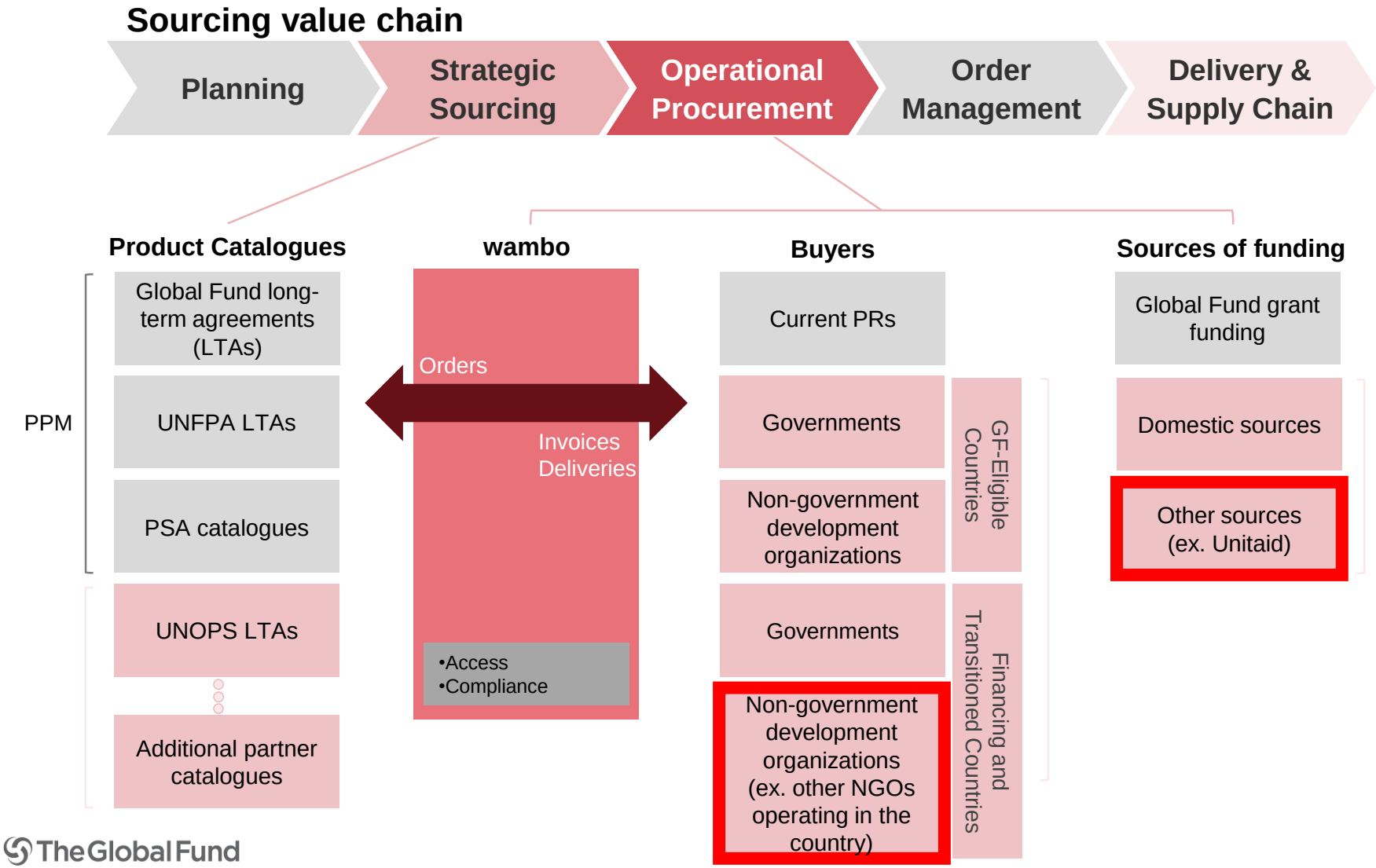
Improved access to **AHD**
(ex. flucytosine)

- GF and Unitaid **leverage volumes**, and procure **flucytosine** through **GF long-term agreements with suppliers** and **wambo platform**. 30,000 packs of flucytosine will be procured.

Global Fund and Unitaid are exploring the opportunities to extend this model of collaboration to other products in the Global Fund PPM portfolio.

Leveraging impact

In November 2019, the Global Fund Board approved a strategy for expanded access to the framework agreements by non-grant buyers using wambo.org

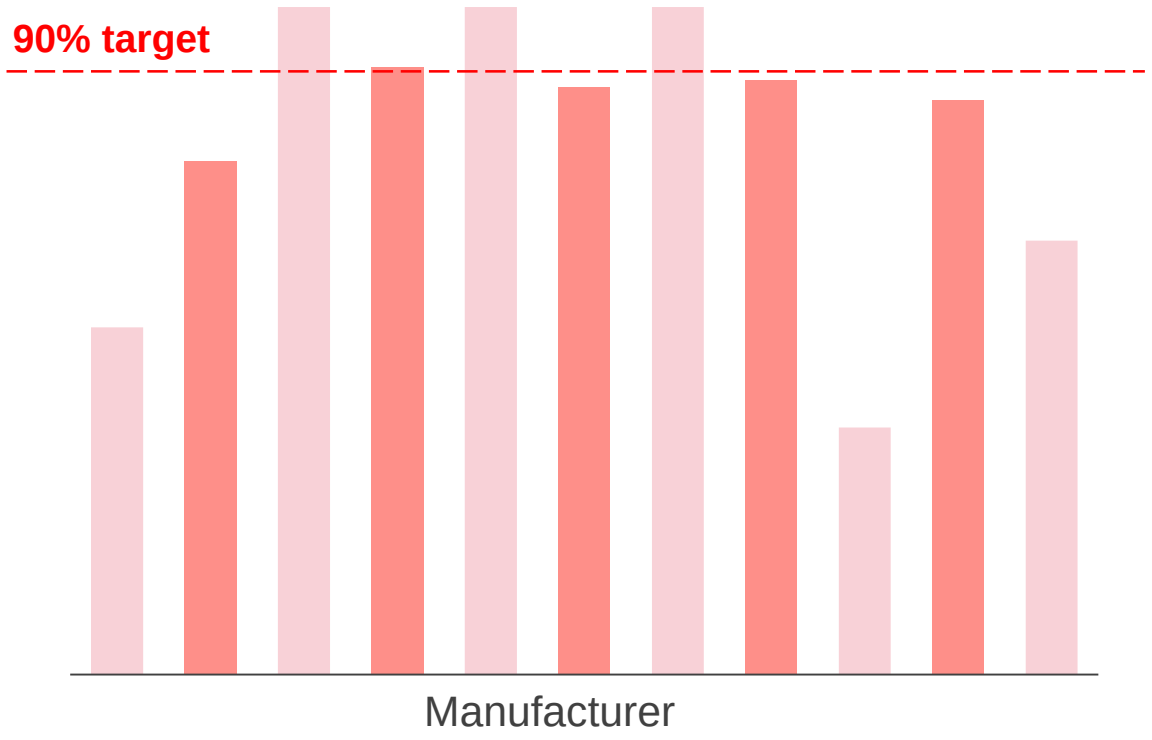


Increased numbers of orders from different sources of funding and different buyers in 2020

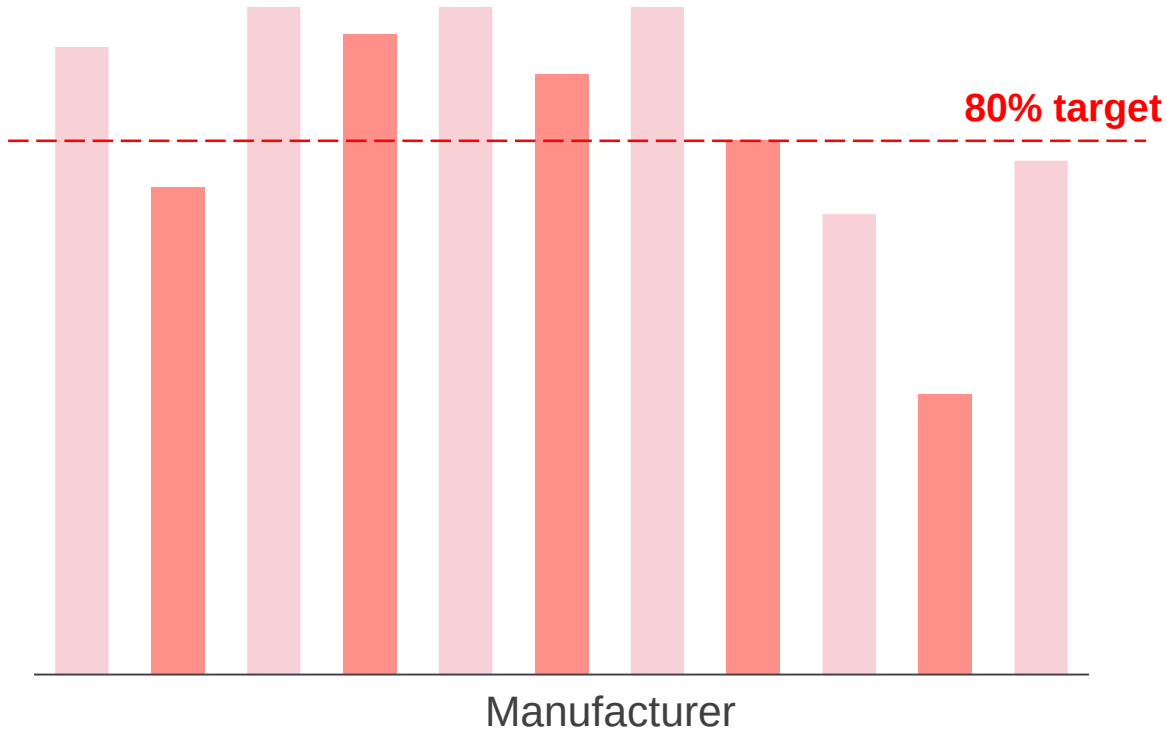
2019 supplier performance at the end of Q3

874 shipments of 51 products to 51 countries

OTIF



Responsiveness



Strengthened reporting for performance management: key measures to mitigate supply risks, increase supply visibility and prompt best practices

Scope:
Some of the measures may only apply for some products

Reporting:
Reports required on annual, quarterly or monthly basis, depending on the specific measure

Confidentiality:
Commercially sensitive information will be kept confidential

Newly eligible products: proactively notify us on new approvals and product commercialization timelines for ARVs and other products covered by agreements

Most Favored Nation (MFN) Clause

- MFN clause in contract supports our efforts to ensure best value for Global Fund
- Proactively manage the principles and implementation of the MFN clause
-
-
-

Planned Capacity

-
-

Production lead time and responsiveness

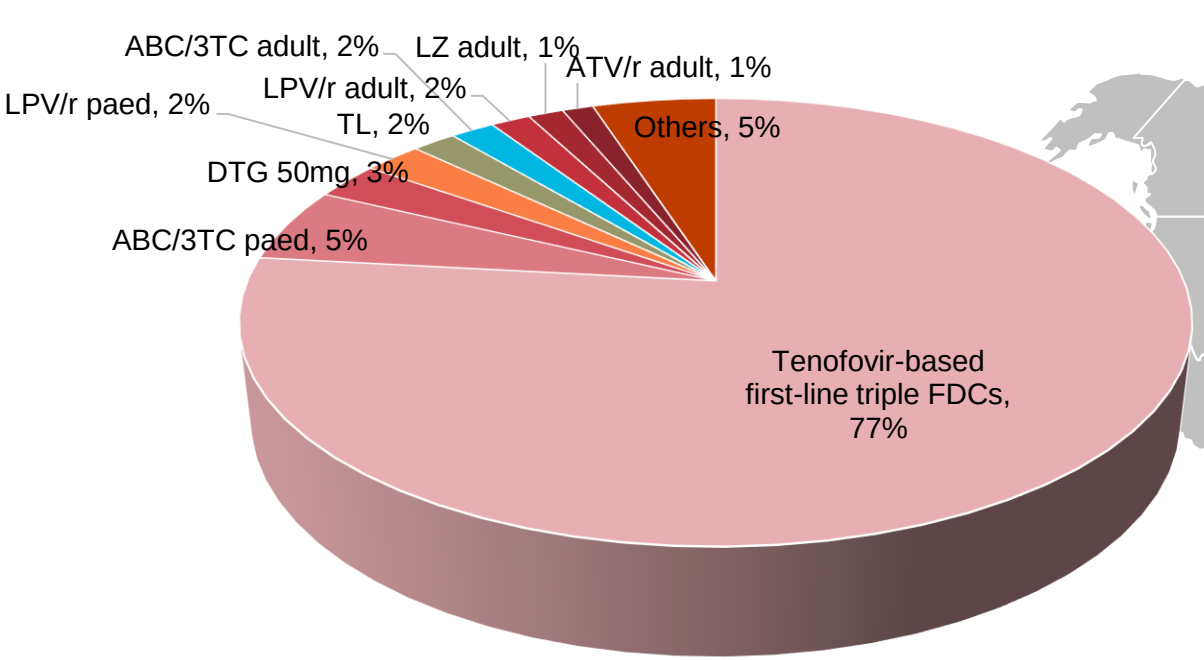
-
-

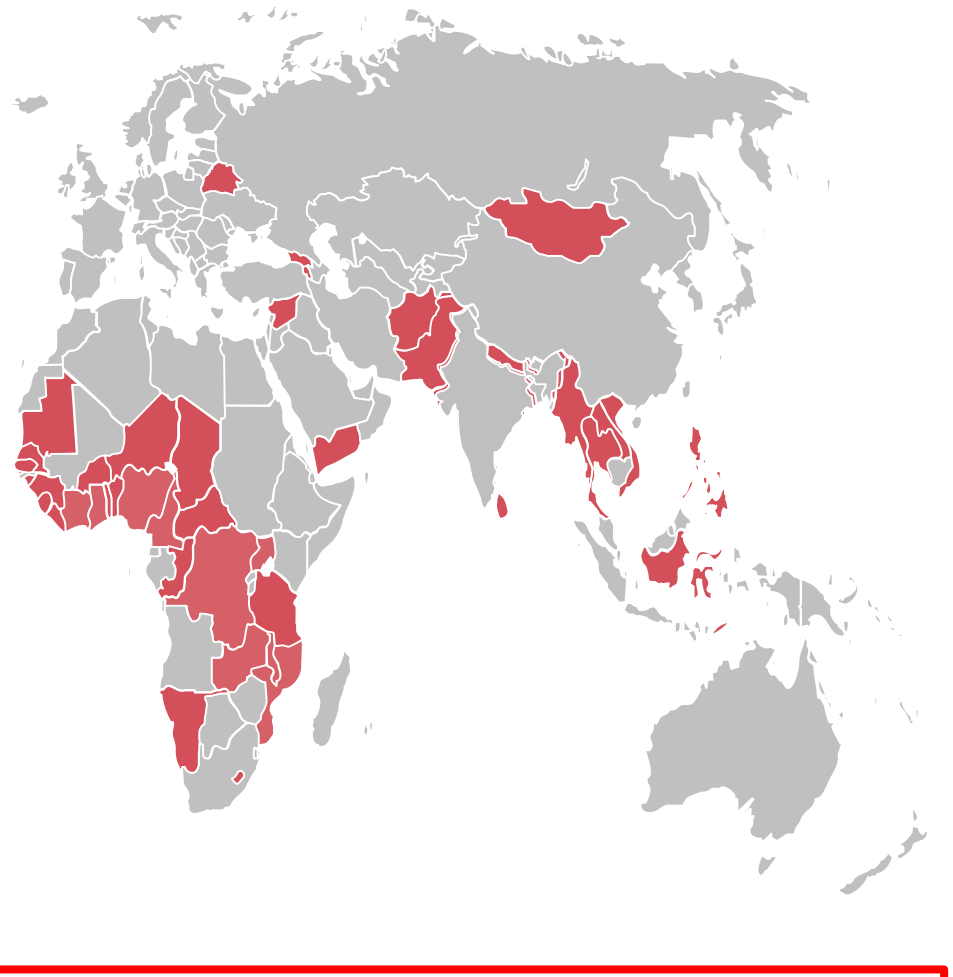
Upstream supply visibility

	Key Starting Materials	Intermediate (INT)	Active Pharmactutiacl Ingredients (API)
Scope	▪ KSM may have impact on supplier security and cost	▪ Registered Intermediate (INT) and APIs in the FPP dossier	
Information required	▪ Name /CAS number ▪ Supplier information ▪ others	▪ Name /CAS number ▪ Supplier information including current registered supplier and suppliers are in the process with indicative approval timeline ▪ others	
Supporting documents	▪ Copy of dossier with regards to the route of synthesis of the API (DMF open part); registered INT and API manufacturers in FPP the dossier; ▪ Varation approval with regards to new API/INT suppliers or new INTs		

Note: We may or may not share information with RSA and USG under mutually agreed confidentiality terms

56 million packs ARVs estimated for 2020 delivery through PPM





More than 90% tenofovir-based FDCs = cartonless for POs placed in 2019

more detailed forecast for 2020 has been published @ https://www.theglobalfund.org/media/7180/ppm_arv2020forecast_table_en.pdf

Afghanistan, Armenia, Belarus, Benin, Burkina Faso, Cote d'Ivoire, Cameroon, Cape Verde, Central African Republic, Chad, Comoros. Congo, Congo DRC, Fiji, Gambia, Georgia, Ghana, Guatemala, Guinea, Guyana, Haiti, Honduras, Indonesia, Jamaica, Laos, Lesotho, Liberia, Malawi, Mali, Mauritania, Mongolia, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Niger, Nigeria, Pakistan. Philippines, Senegal, Sierra Leone, Sri Lanka, Syrian Arab Republic, Tanzania, Thailand, Timor-Leste, Togo, Uganda, Vietnam, Yemen, Zambia

Active supplier performance management with a greater focus on supply security, OTIF & responsiveness

- Performance is reviewed on a quarterly basis with allocation/commitment adjusted annually
- Opportunity for incremental gain (or loss) of volume

Phase I Revised allocation base	Phase II Reallocate pooled volume	Phase III Implemention risk assessment	Phase IV Performance mgmt. & allocation adjustment
▪ Tender outcome informs the initial allocation base ▪ Supplier allocation base revised based on performance compared to target ▪ Volume pool created from under performance	▪ Reallocate pool volume through defined mechanism based on over-performance	▪ Range of risk factors considered including quality & other implementation constraints (pricing, registration footprint, long lead-times) ▪ Allocation finalized with risk mitigation plan	▪ Actual allocation may be adjusted according to performance and any emerging implementation challenges

Well-defined consistent approach and rules applied

The Global Fund's 2019 Sixth Replenishment Conference pledged US$14.02 billion for the next three years to save 16 million lives and to end the epidemics of AIDS, tuberculosis and malaria by 2030.

More information: http://www.theglobalfund.org/en/sourcing/info/

- Overview
- Updates
- Market Shaping Strategy
- Procurement Tools
- **Health Product Procurement**
  - Antimalarial Medicines
  - Antiretrovirals
  - HIV & Malaria Rapid Diagnostic Tests
  - Long-Lasting Insecticidal Nets
  - Other Essential Medicines
  - Procurement Services
  - Viral Load & Early Infant Diagnosis
- Information for Suppliers

Health Product Procurement

The Global Fund plays a significant role in global markets for health products used in the fight against the three diseases. As a key financier in public health, we are committed to maximizing our investments through achieving affordable, quality assured, timely delivered health and medical products.

83%

IN-COUNTRY ON-TIME-IN-FULL DELIVERIES IN 2018

We regularly update our procurement planning and budgeting guides with indicative lead times for key health products and health technologies, as well as estimated freight, insurance and quality assurance costs:

- Category and Product-Level Procurement and Delivery Planning Guide: Indicative Lead Times
  download in English | Français
- Pooled Procurement Mechanism: Freight, Insurance, Quality Assurance/Quality Control Indicative Reference Costs
  download in English

We actively engage in global markets for key medicines and health products used in the fight against the three diseases, and have established long-term framework agreements with suppliers in several product categories. Product category specific information, procurement strategies and past tender documents can be found on each product category page:

Global Supply Chain
GHSC-PSM ARV Update

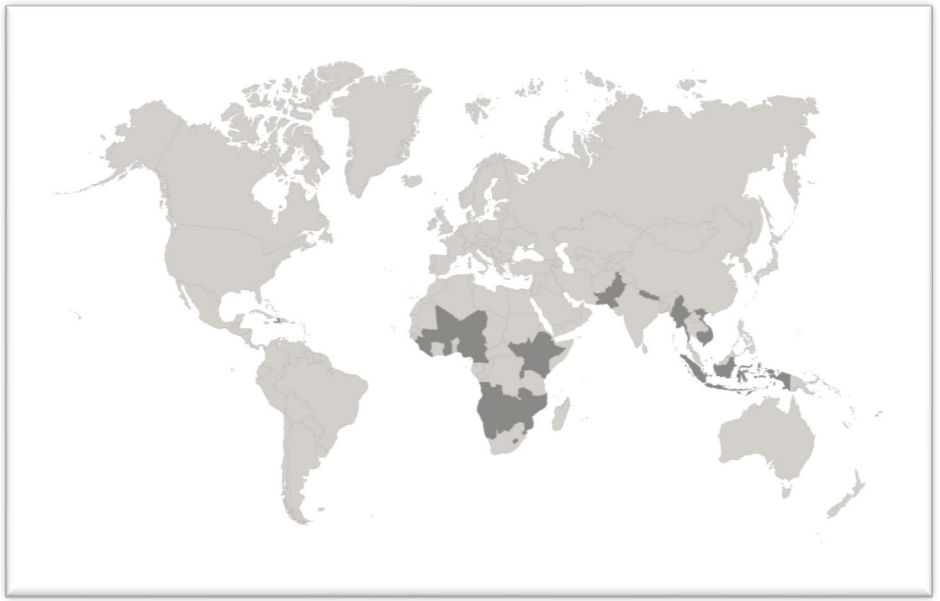
Alan Pringle
Global Supply Chain Director

USAID GLOBAL HEALTH SUPPLY CHAIN PROGRAM
Procurement and Supply Management (GHSC-PSM)

USAID
FROM THE AMERICAN PEOPLE

PEPFAR
U.S. President's Emergency Plan for AIDS Relief

USAID GLOBAL HEALTH SUPPLY CHAIN PROGRAM



34 Country/Regional Offices
3 Regional Distribution Centers

All figures are over the life of the project unless otherwise indicated as of June 30 2019.

ON TARGET

92%
ON TIME DELIVERY
in Q3, FY2019

$193 M
DELIVERED
in Q3, FY2019

$2 B
of commodities
DELIVERED

$95+ M
COST SAVINGS*
on commodities and logistics

ON THE MOVE

6,000+
SHIPPING LANES

5
INTERNATIONAL FREIGHT FORWARDERS

300+
SUPPLIERS

17
DELIVERIES*
every day

4,000+
ITEMS
in the product catalog

LOCAL FOOTPRINT

1,200
COUNTRY OFFICE STAFF

43
COUNTRIES
received technical assistance

$249.7 M
PROCURED
through local channels

34%
LINE ITEMS
procured through local channels

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PEPFAR U.S. President's Emergency Plan for AIDS Relief

Forecasting Increasingly Driven by Data Analytics

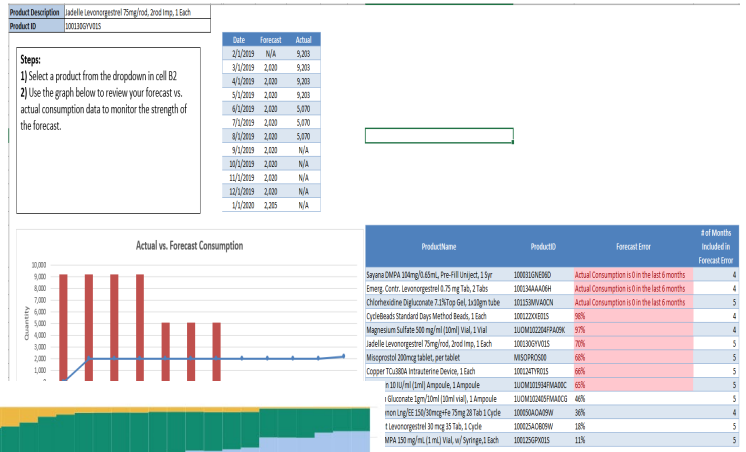
Country Based Supply Plans

Forecasting and Supply Planning Team – Quality Check

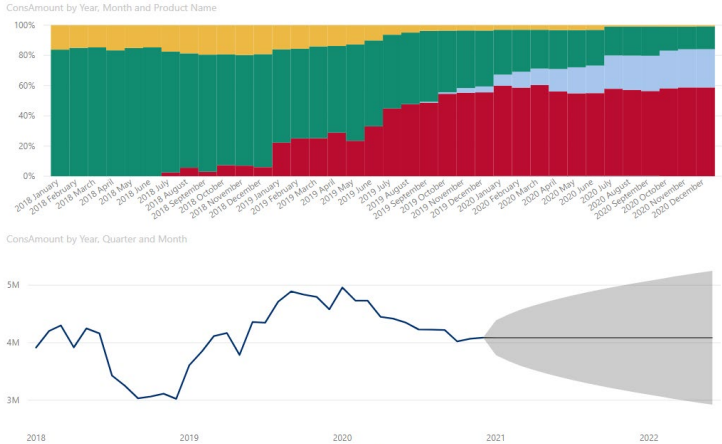
Plan Team – Global Aggregation and Order Planning

Suppliers – Information shared on a Quarterly Basis

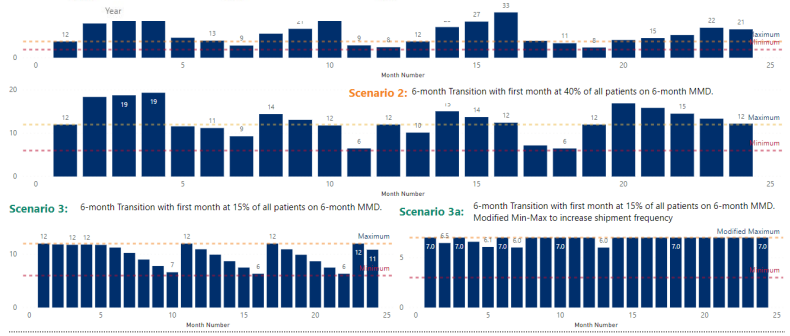
Data Quality Check Automation and Feedback



Modeling of Transitions



Scenario Planning



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ARV Sourcing Strategies Driven by Product Characteristics

Timing of Sourcing Events

Long Term Agreements (LTA)

- Contracts establish working terms and conditions between the legal entities

Multi-Year w Options

TLD Procurements

- Working under LTA, tender events are done quarterly
- Regular tenders allow for new entrants
- Firm orders placed for a rolling 12 months of Goods Availability Dates

Quarterly

Standard Procurements - Allocation

- Working under LTA, tender events are done annually
- Firm fixed-prices established for 12-month period
- Primary sources identified annually to streamline process as country orders are received and purchase orders placed
- Primary Sources clustered by API

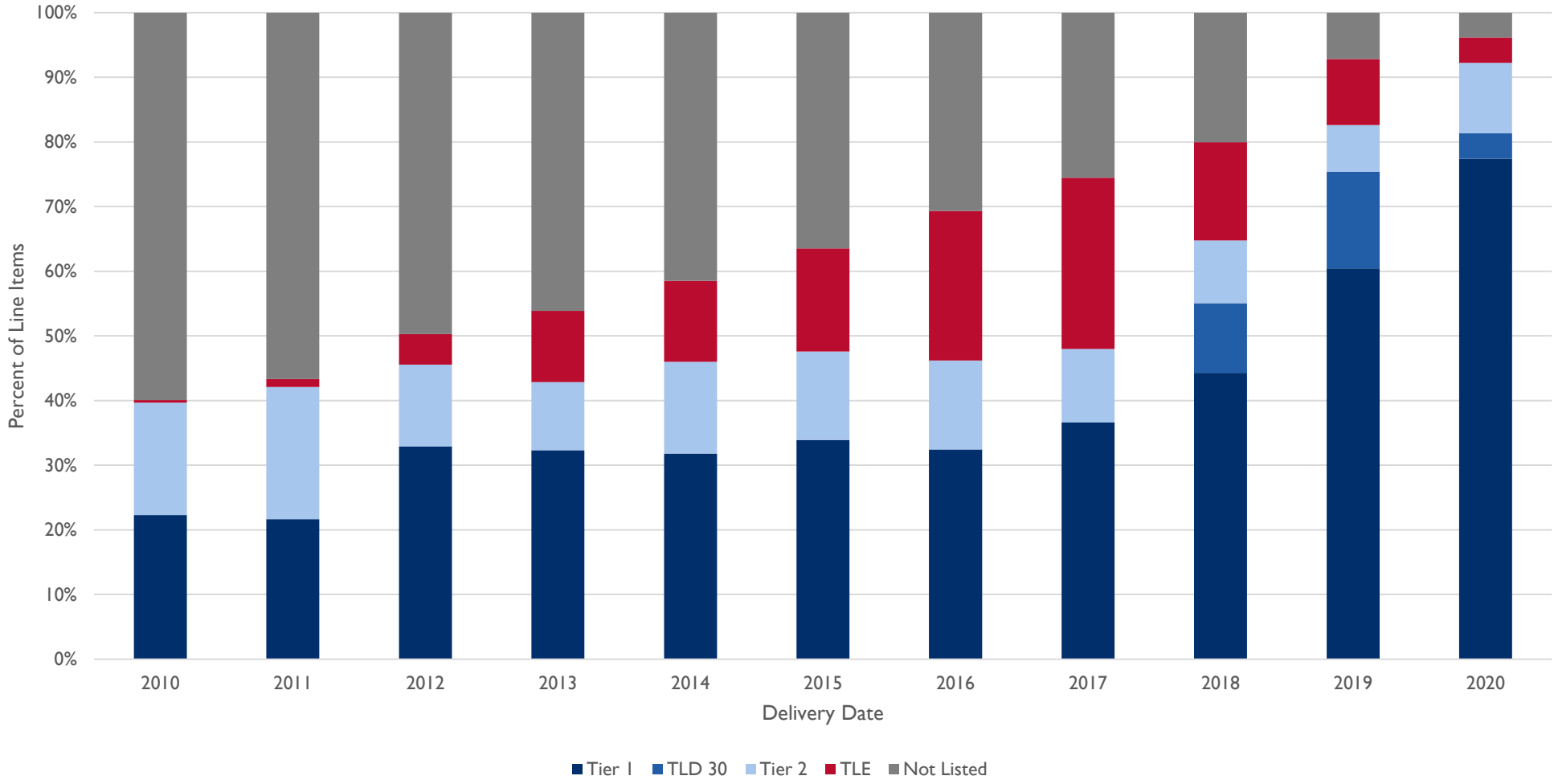
Annually

Regular market interaction for TLD and predictable sourcing elsewhere satisfies dynamic product needs

Data Driven Proactive Order Management Process

Product_Group	Sub Category	Country	ProductID	PSM SKU	Product Name	Requested Delivery Date	Target Order Entry Date	Time to Order (Weeks)	Order Type	Max Lead Time (Weeks)	Funds	Quantity	Shipment MOS	UOM StartBalance	MOS_on_RDD
ARV	Adult ARV	X	102762AAA07U	102762AAA07U	TLD 50/300/300 mg Tablet, 90 Tablets	12/13/2019	5/3/2019	-5.8	RDC	32	PSM	57,613	15.5	-	-
ARV	Adult ARV	X	100111AAA	100111AAA07P	Etravirine [Intelence] 100 mg Tablet, 120 Tablets	1/31/2020	6/21/2019	-4.2	Direct Drop	32	TBD	1,374	6.7	669	3.3
ARV	Adult ARV	X	100023AAA	100023AAA07G	Lamivudine 150 mg Tablet, 60 Tablets	6/30/2020	11/19/2019	0.9	Direct Drop	32	PSM	1,571	6.2	941	3.7
ARV	Pediatric ARV	X	100116AAA	100116AAA07G	Lamivudine/Zidovudine 30/60 mg Tablet, 60 Tablets	6/30/2020	11/19/2019	0.9	Direct Drop	32	TBD	1,930	4.2	2,632	5.8
ARV	Adult ARV	X	101833AAA	101833AAA07G	Raltegravir [Isentress] 400 mg Tablet, 60 Tablets	6/30/2020	11/19/2019	0.9	Direct Drop	32	PSM	1,323	6.6	671	3.4
ARV		X	100846DGA	100846DGA0CS	TLD 50/300/300 mg Tablet, 90 Tablets	6/30/2020	11/19/2019	0.9	RDC	39	PSM	1,105	5.6	837	4.3
ARV	Adult ARV	X	101679AAA	101679AAA06Z	Dolutegravir 50 mg Tablet, 30 Tablets	7/31/2020	12/20/2019	1.9	Direct Drop	32	PSM	10,735	5.4	8,758	4.4
ARV	Adult ARV	X	100101AAA	100101AAA06Z	Abacavir/Lamivudine 600/300 mg Tablet, 30 Tablets	7/31/2020	12/20/2019	1.9	Direct Drop	32	TBD	5,561	3.7	9,319	6.2
ARV	Adult ARV	X	100106AAA	100106AAA07G	Darunavir 600 mg Tablet, 60 Tablets	7/31/2020	12/20/2019	1.9	Direct Drop	32	PSM	2,017	7.6	627	2.4
ARV	Pediatric ARV	X	100858AAA	100858AAA07G	TLD 50/300/300 mg Tablet, 90 Tablets	7/31/2020	12/20/2019	1.9	RDC	32	TBD	210	5.4	167	4.3
ARV	Pediatric ARV	Y	102006AAG	102006AAG07G	Raltegravir [Isentress] 25 mg Chewable Tablet, 60 Tablets	7/31/2020	12/20/2019	1.9	Direct Drop	32	PSM	490	7.1	177	2.6
ARV	Pediatric ARV	Y	100107AAA	100107AAA09Q	Darunavir [Prezista] 75 mg Tablet, 480 Tablets	7/31/2020	12/20/2019	1.9	Direct Drop	32	PSM	240	6.2	137	3.5
ARV	Pediatric ARV	Y	103181AAK	103181AAK06Z	Abacavir/Lamivudine 120/60 mg Dispersible Tablet, 30 Tablets	7/31/2020	12/20/2019	1.9	Direct Drop	32	PSM	2,020	5.9	1,286	3.8
ARV	Adult ARV	Y	100027AAA	100027AAA07P	Lopinavir/Ritonavir 200/50 mg Tablet, 120 Tablets	9/30/2020	1/1/2020	2.3	RDC	32	PSM	6,182	4.5	7,484	5.5
ARV	Pediatric ARV	Y	100032DGK	100032DGK04S	TLD 50/300/300 mg Tablet, 90 Tablets	8/31/2020	1/20/2020	2.9	Direct Drop	32	TBD	2,440	4.8	2,646	5.2
ARV	Adult ARV	Z	100110AAA06Z	100110AAA06Z	Emtricitabine/Tenofovir DF 200/300 mg Tablet, 30 Tablets	8/31/2020	1/20/2020	2.9	Direct Drop	43	PSM	59,910	5.6	9,086	0.9
ARV	Pediatric ARV	Z	103181AAK07G	103181AAK07G	Abacavir/Lamivudine 120/60 mg Dispersible Tablet, 60 Tablets	8/31/2020	1/20/2020	2.9	RDC	43	TBD	100,000	1.4	171,040	2.5
ARV	Adult ARV	Z	101679AAA06Z	101679AAA06Z	Dolutegravir 50 mg Tablet, 30 Tablets	8/31/2020	1/20/2020	2.9	RDC	43	PSM	80,320	1.2	441,894	6.6

Catalogue Management Driving Optimized Formulary



Data Driven Performance Management

Continuous Improvement

- Performance Improvement Plans
- Senior executive visibility
- Escalation process for issue resolution

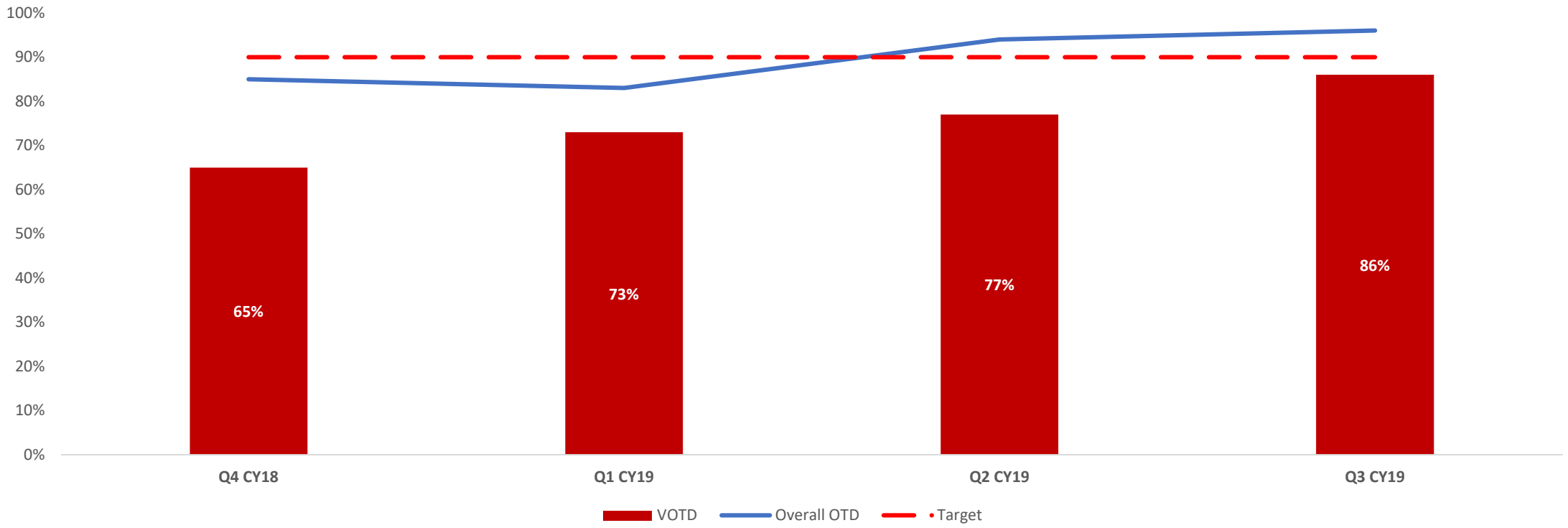
Metrics & Scorecard

- Contractually establishes metrics
- Metrics measured monthly
- Shared and reviewed by suppliers before the QBR

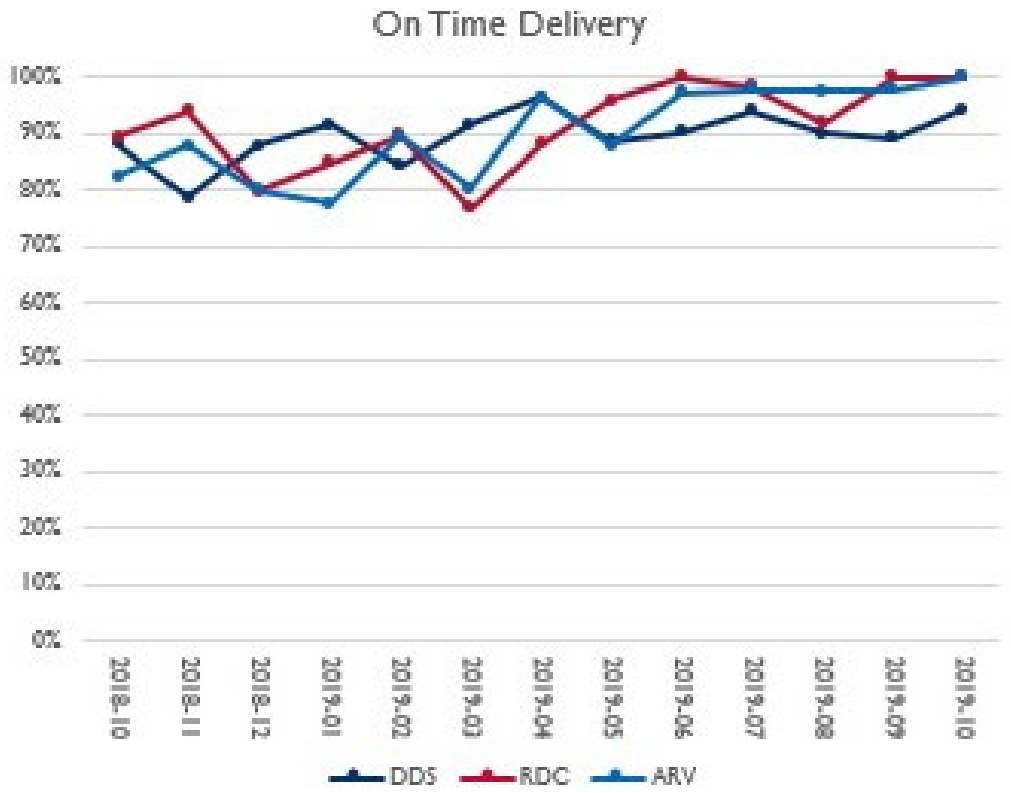
Quarterly Business Reviews

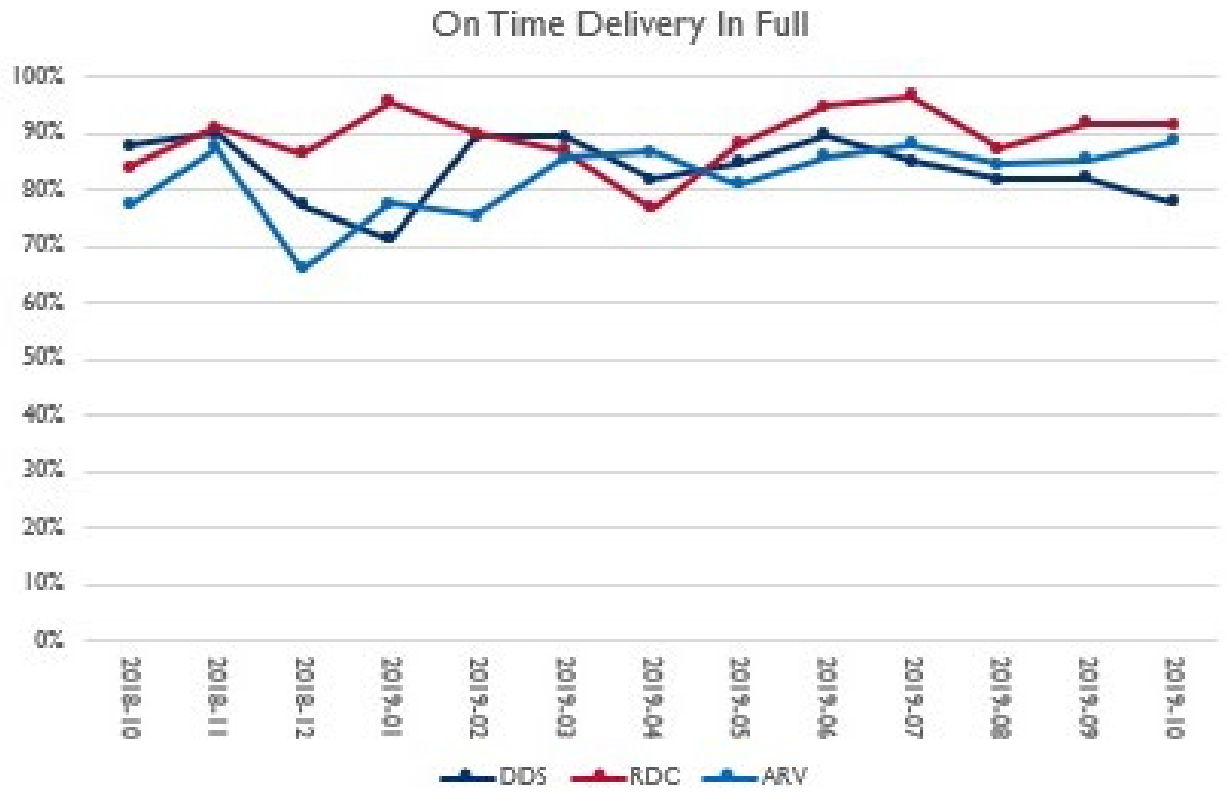
- Executive-level, quarterly review focused on the strategic direction of the relationship
- Key stakeholders and executive level supplier participation

Suppliers OTD Increasing Contribution to Overall Success



OTD ≥ 90% seven straight months & OTIF ≥ 80% eight months





Thank You!

Consolidated Forecast of Global ARV Demand: Scenarios, Data and Forecasts 2018 – 2023

John Stover and Adebiyi Adesina: Avenir Health

For the Forecasting Technical Working Group: WHO, UNICEF, CDC, CHAI, USAID-GHSC, Global Fund, UNAIDS, USAID, UNITAID, MPP, Avenir Health

Purpose

- Forecast numbers of patients on ARVs and demand for individual ARVs in low and middle-income countries for 2018 to 2023 using best available evidence.

- Data sources include:
  - WHO ARV Survey
  - CHAI projected regimen data (Adults on First-line only)
  - MPP projected regimen data UNAIDS projections of need for ART (Fast-Track)
  - UNAIDS and Spectrum/EPP estimated number of people on ART

Outline

- Comparing linear projection to observed number of people on treatment
- Methodologies of projections used to estimate for number of people on treatment.
- Estimated number of adults and children on first and second line.
- Proportion of adults and children on second line
- Adult market data
  - Adult API regimen market share projections
  - Total API demand volume in person-years
- Paediatric market data
  - Paediatric API regimen market share projections.

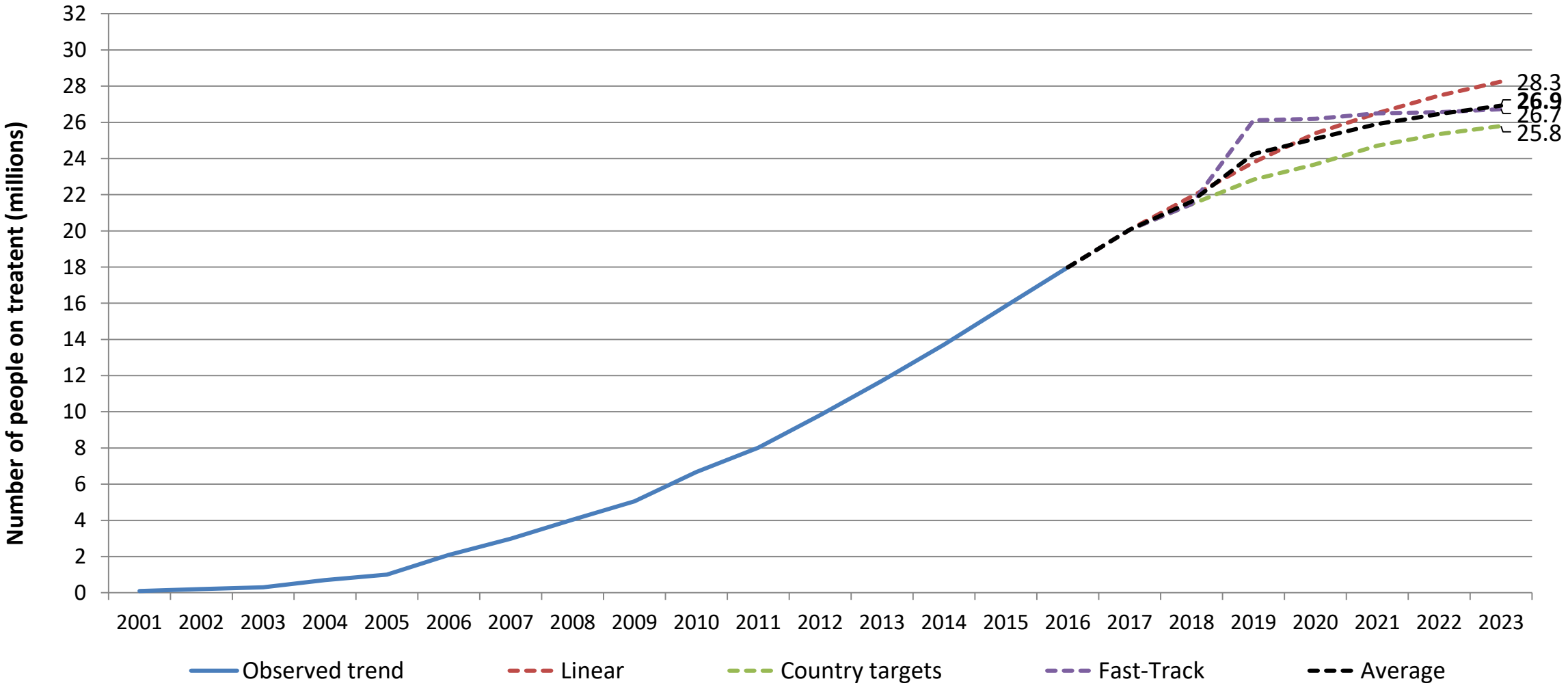
Projection Methods: Number on ART

Linear extrapolation: Linear extrapolation of last three years of UNAIDS/WHO reported data on the number receiving ART for 154 low- and middle-income countries.

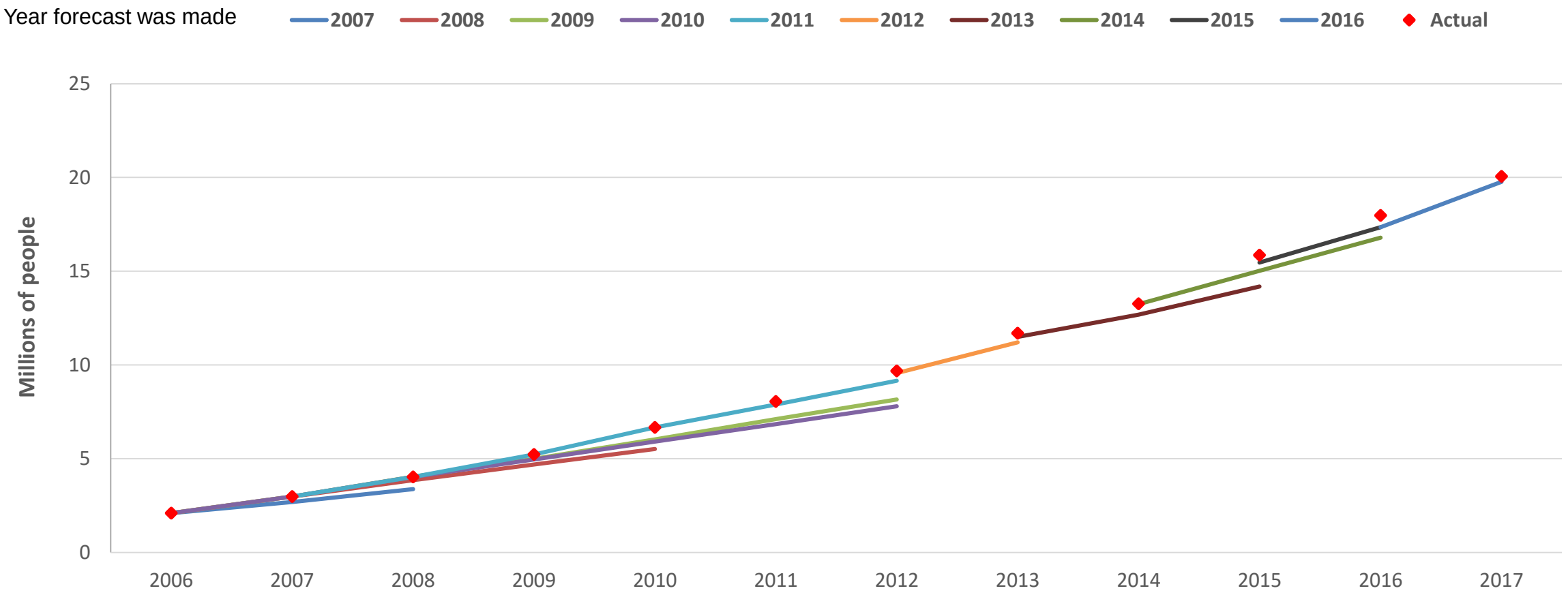
Country targets: ART demand up to 2023 extrapolated from 2017 baseline demand using national targets stated by 62 countries, from the 2018 WHO ARV survey, scaled up to all LMIC.

Fast Track: Projected number of people in LMI countries on treatment assuming that 90% of PLHIV are identified and aware of their status, 90% of whom are started on treatment, and 90% of those on treatment are retained on treatment and achieve viral suppression by 2020.

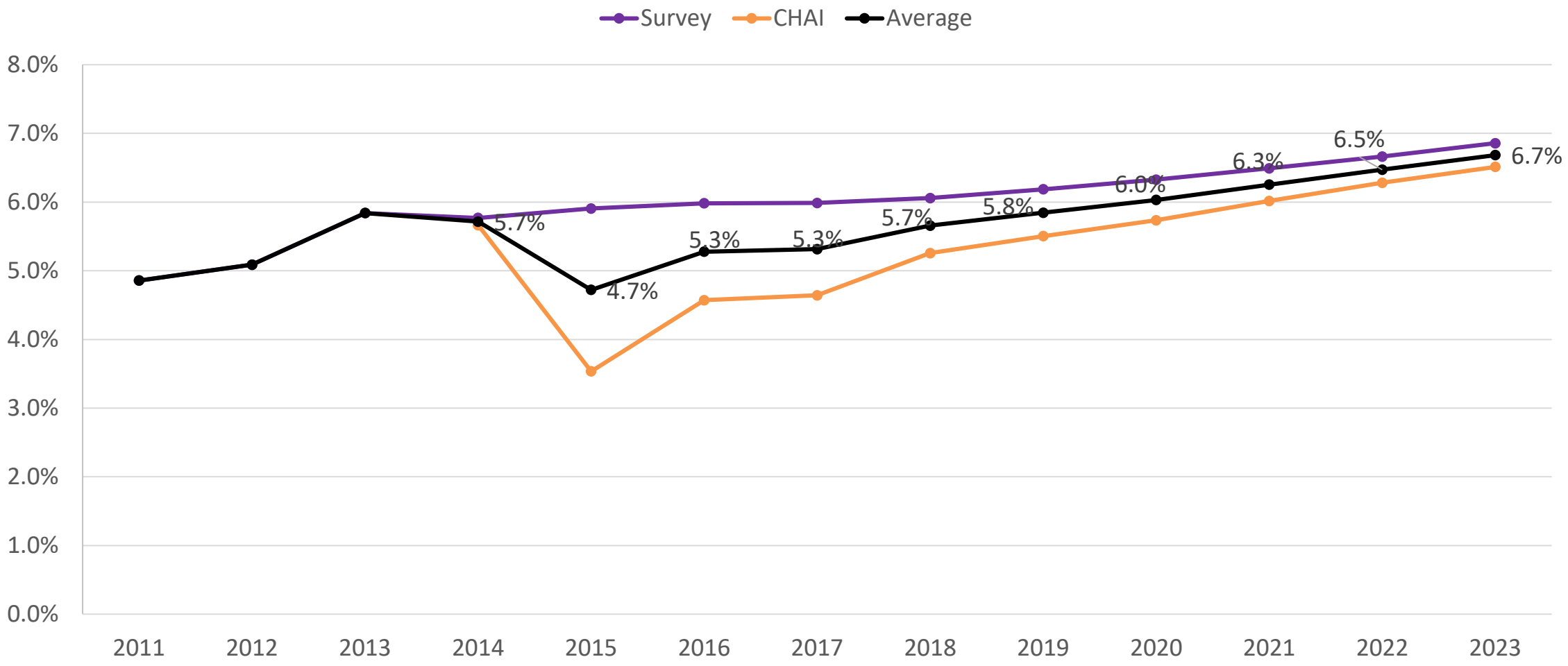
Projected Number of Adults and Children on ART in LMIC: Linear, Country Target and Fast Track Projections and Average



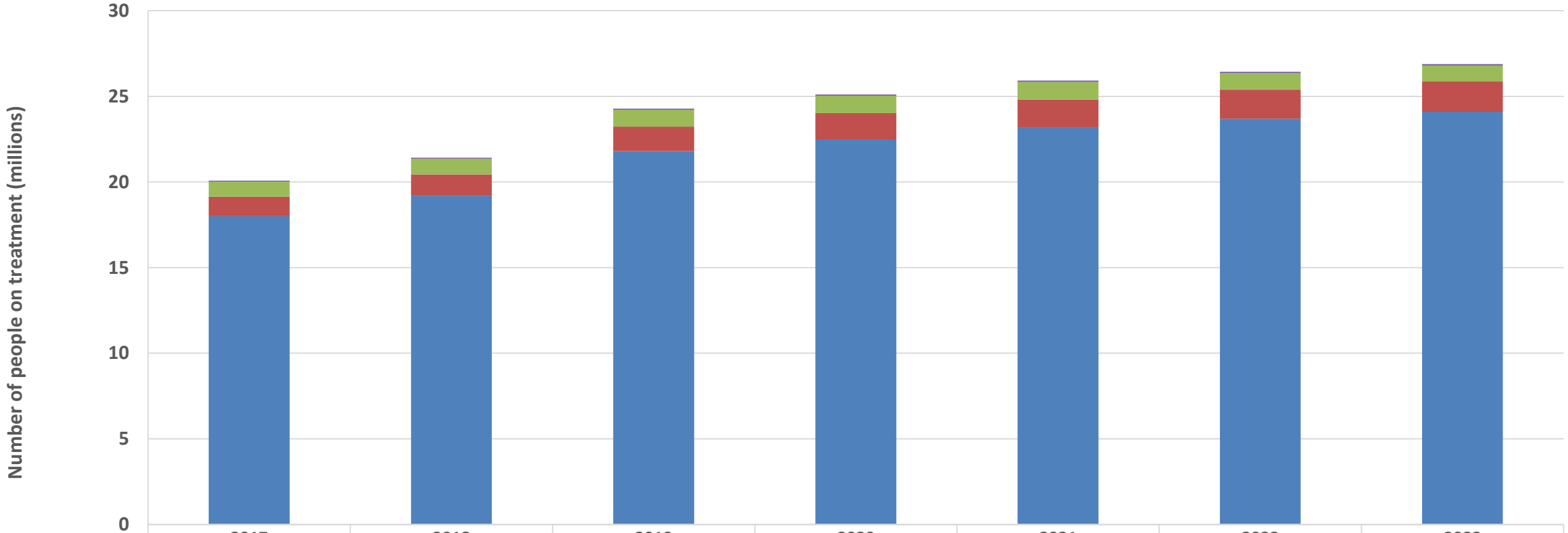
Forecast vs. reality: the gap between linear projections and actual has been decreasing in the last year.



Percent of Adults on Second Line Regimens



Historical and Projected Average Number on ART in LMIC based on Linear, Country target and Fast Track



	2017	2018	2019	2020	2021	2022	2023
Children, second line	62 000	67 000	75 000	83 000	90 000	89 000	92 000
Children, first line	880 000	910 000	980 000	1010 000	1020 000	960 000	920 000
Adult, second line	1 140 000	1 240 000	1 430 000	1 520 000	1 610 000	1 690 000	1 780 000
Adult, first line	18 000 000	19 200 000	21 800 000	22 500 000	23 200 000	23 700 000	24 100 000

UNAIDS World Health Organization Avenir Health

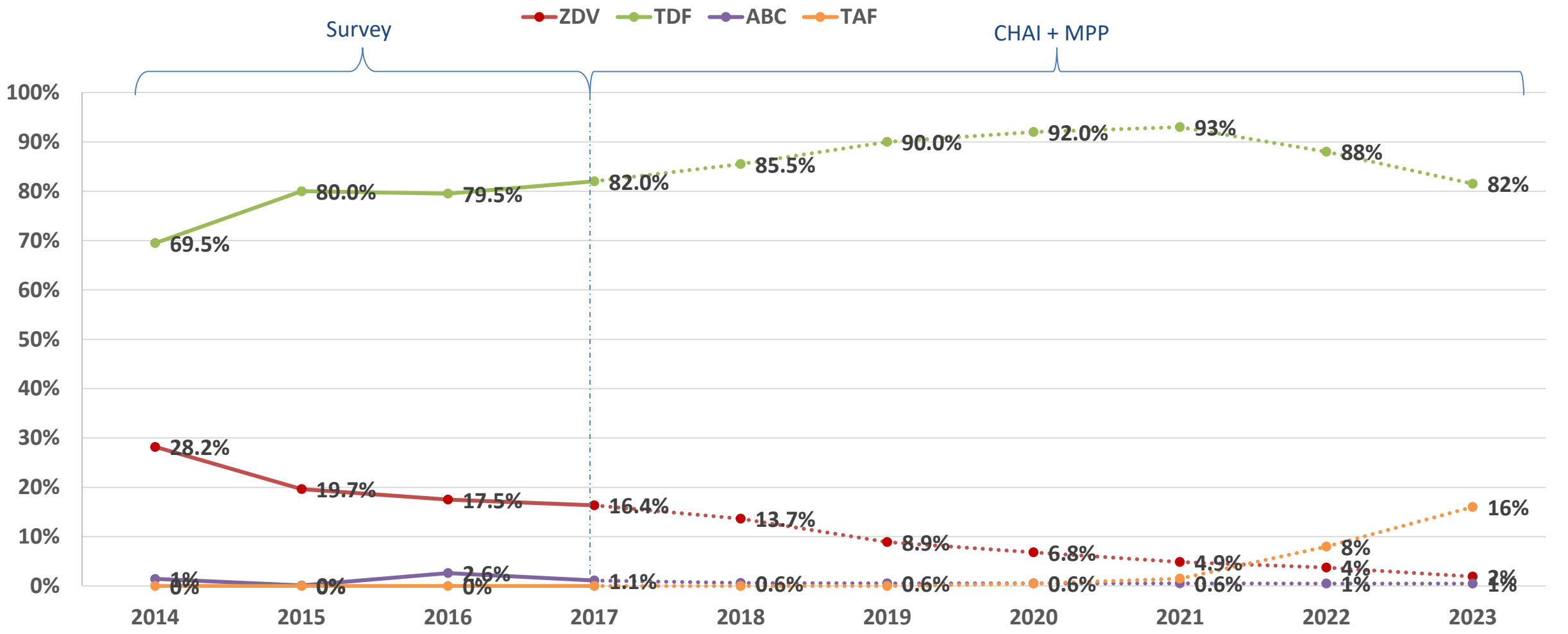
API Distribution for Adult Patients

This distribution of ARV regimens were then categorized into 2 zones:

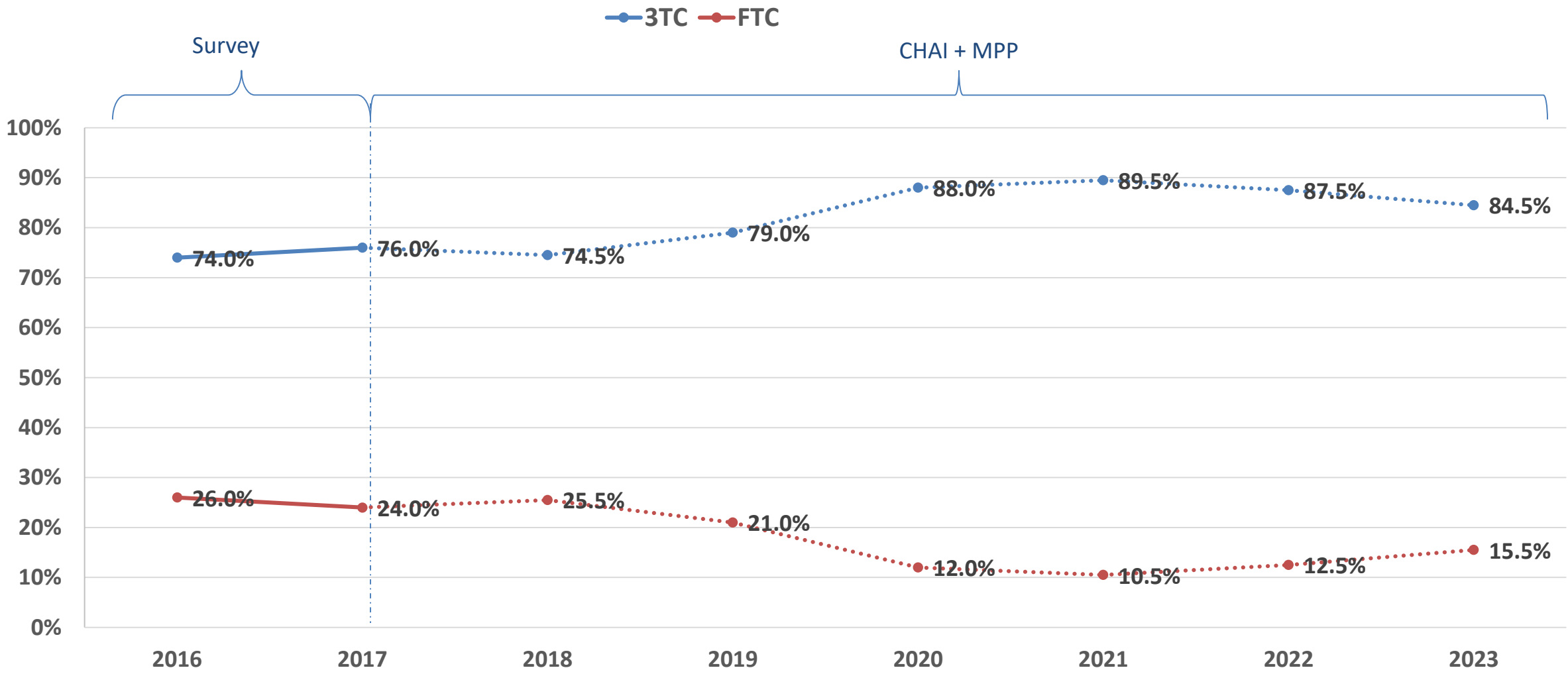
1. Historical data: Based on survey data for 2011-2017

2. Projected PPY data based on consolidated regimen market share data from CHAI and MPP which were then applied to average projected number of adults on treatment from 2018 to 2023.

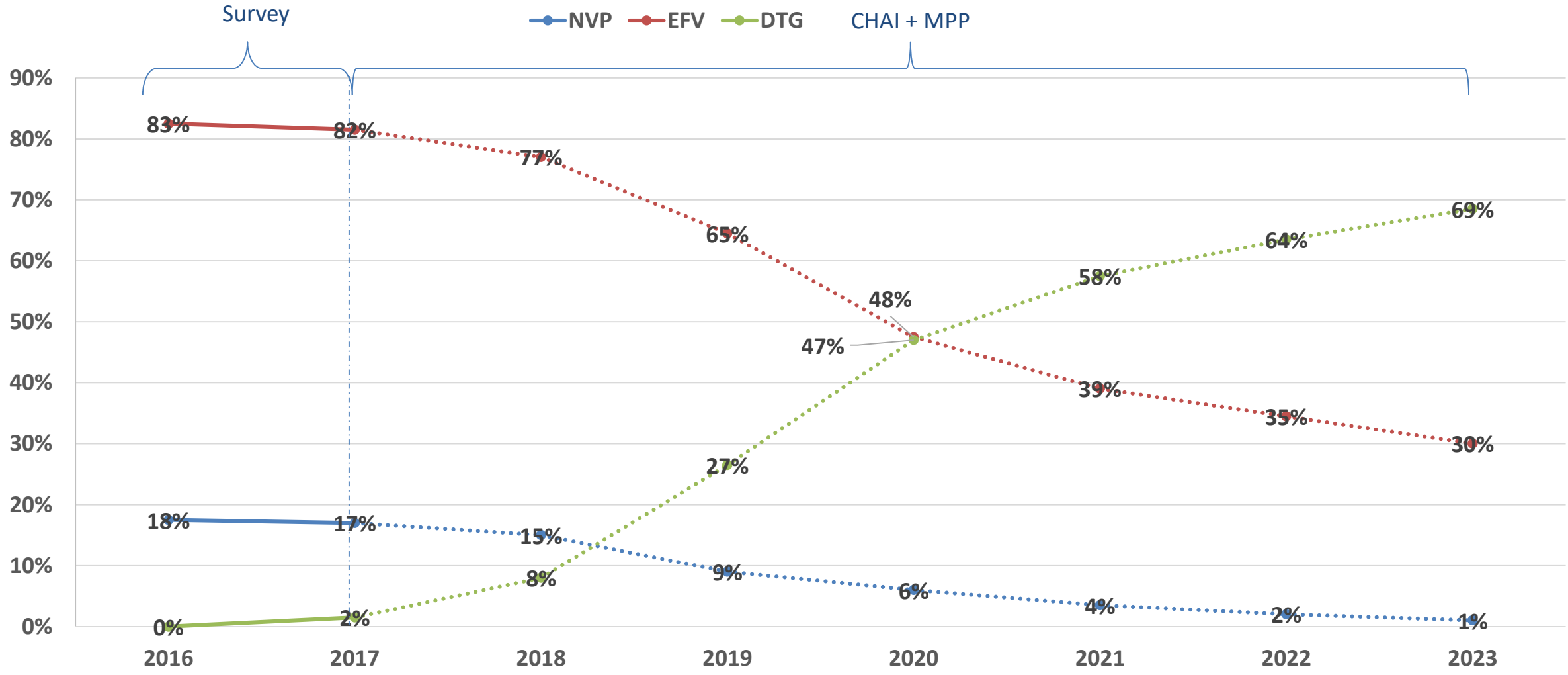
Adult Primary NRTIs (d4T, ZDV, TDF,ABC and TAF)



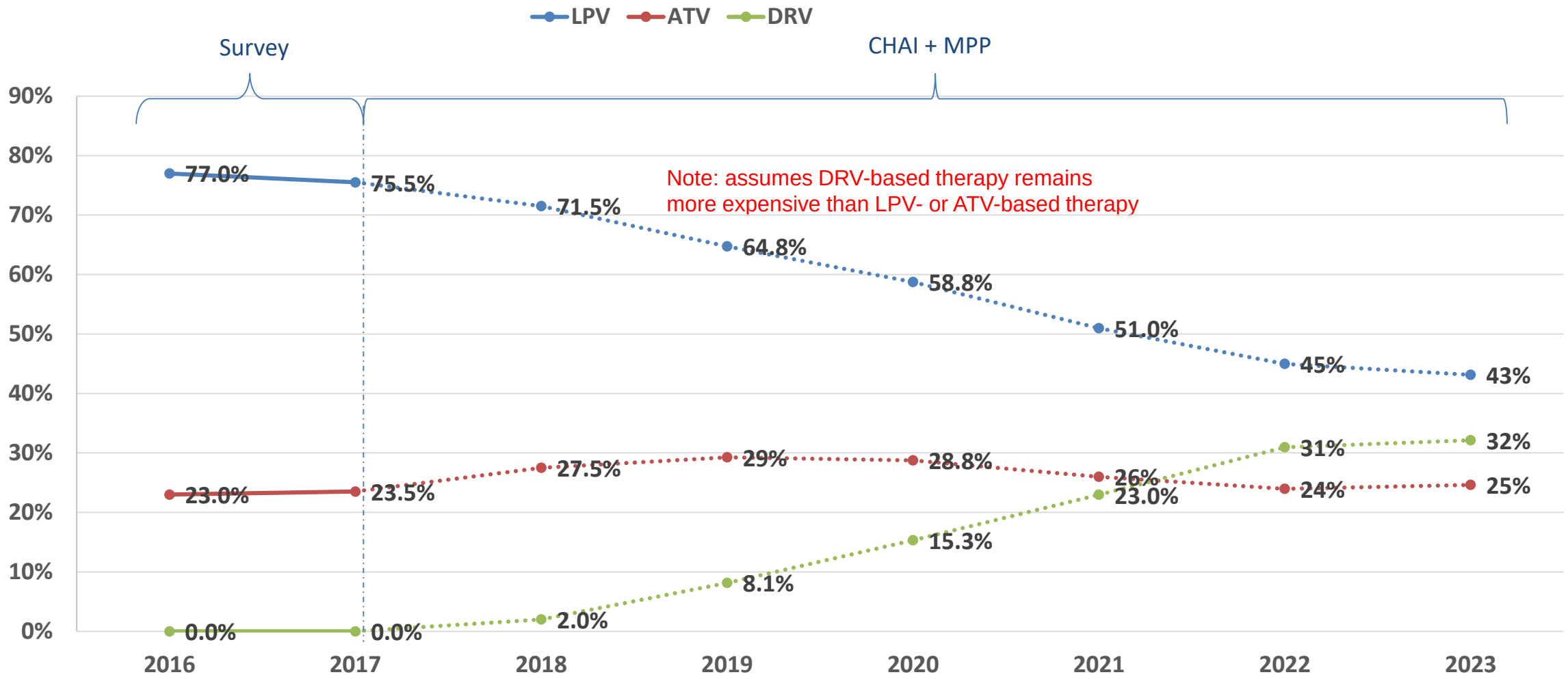
3TC and FTC Share of Adult Secondary NRTIs



NNRTI and DTG Share of Adult market



Adult Share of PIs



Summary - Adult API Market

- Continued growth in numbers of people on ART, adding about an average of 1.5 million per year until 2023
- Slow but steady increase in proportion of adults on second line regimens – however, DTG use in 1L may reduce migration rates to 2L
- Despite expectations that d4T will disappear, there are concerns some countries continue to report a negligible number of patients are on d4T-based regimens.
- NVP market share replaced largely by DTG, with DTG estimated to cover over 50% of the market by 2021.
- ATV share is expected to peak at about 30% of the adult market with expected sharp uptake DRV between 2018 and 2023.

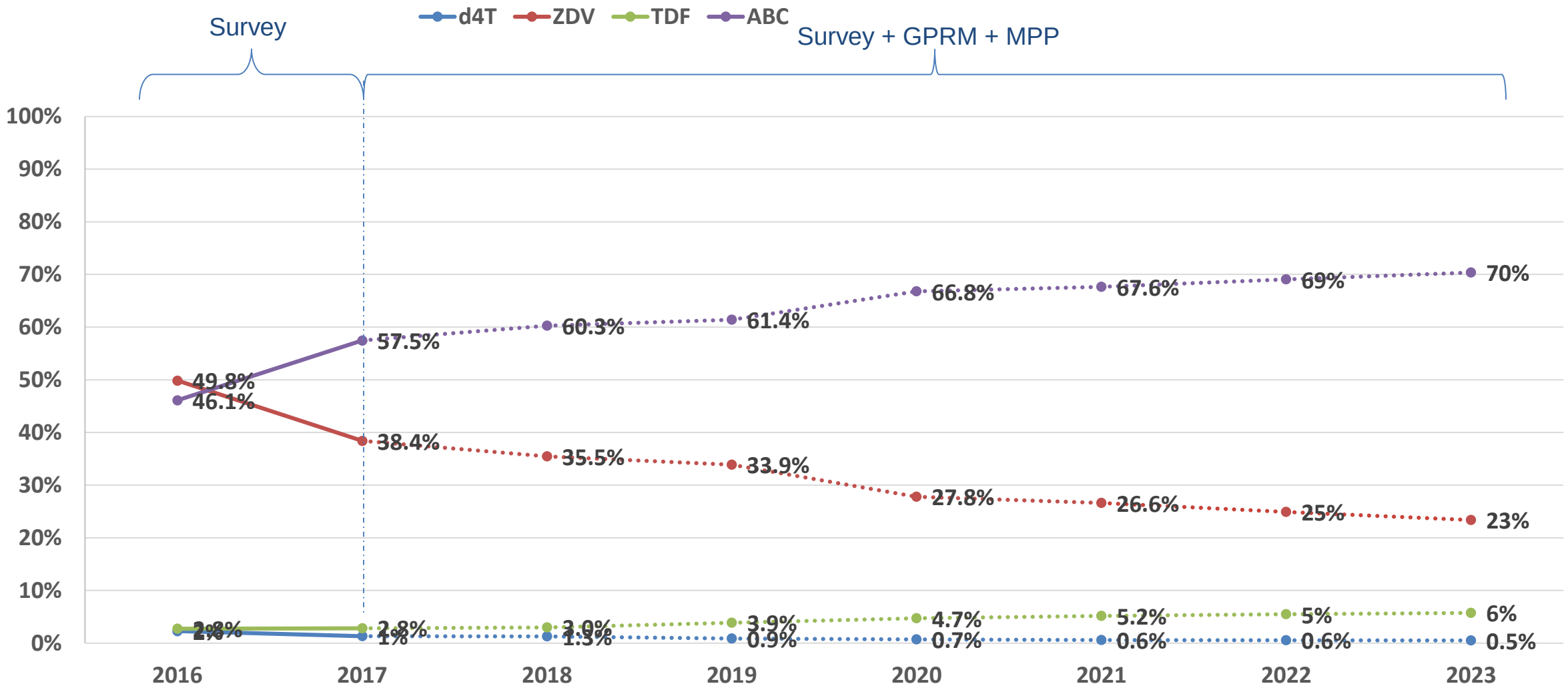
API Distribution for Paediatric Patients

This distribution of ARV regimens were then categorized into 2 zones:

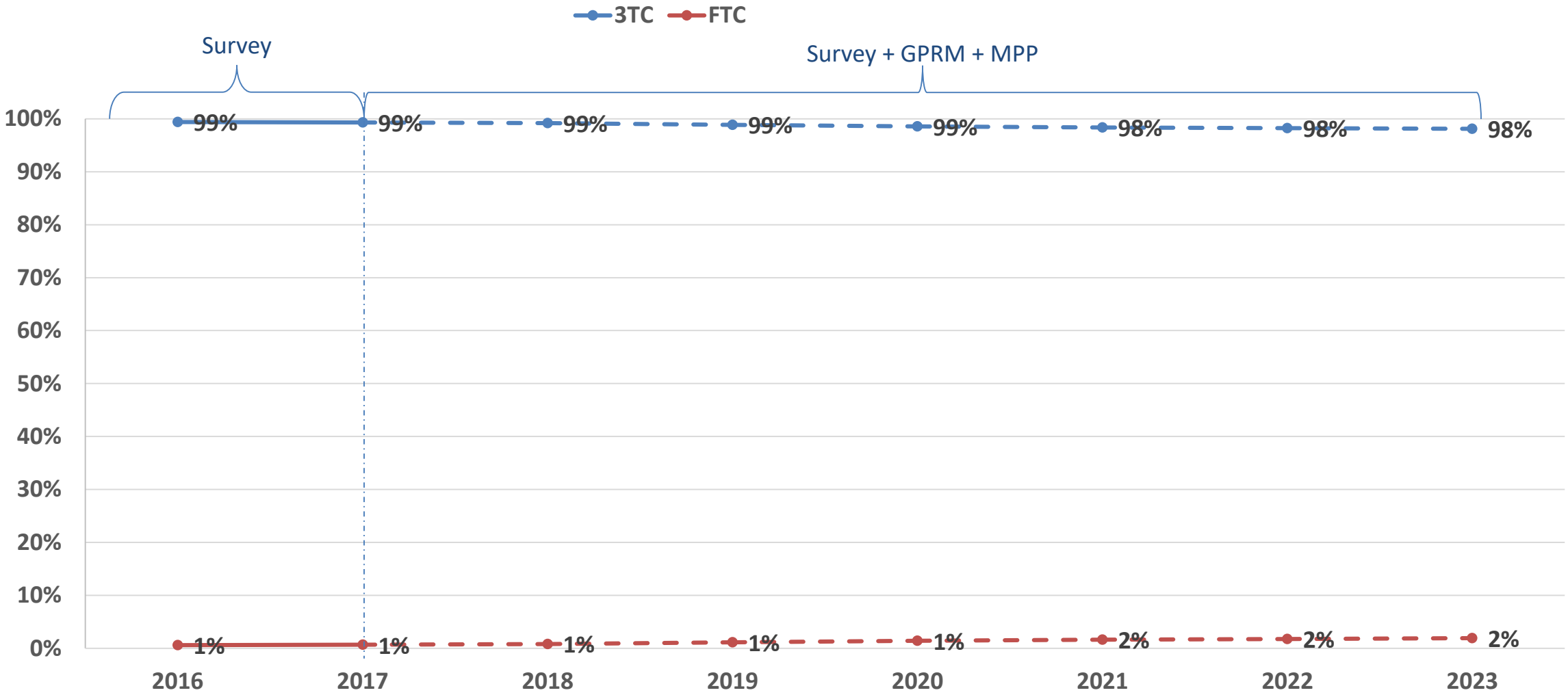
1. Historical data: Based on survey data for 2011-2017

2. Projected PPY data based on consolidated regimen market share data from Survey, GPRM and MPP which were then applied to average projected number of paediatric patients on treatment from 2018 to 2023.
   - Does not include projections for pediatric DRV and TAF due to high uncertainty bounds with a relative small patient base

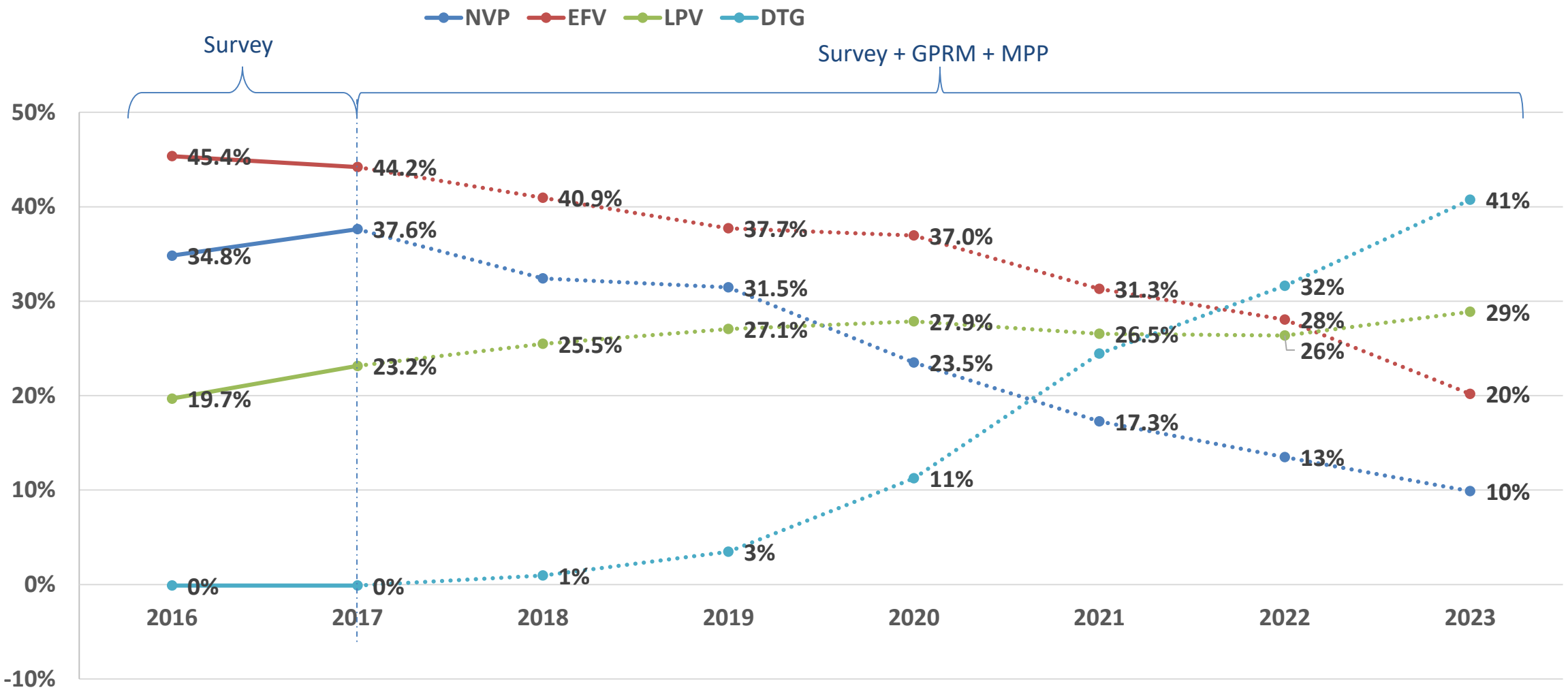
Paediatric Primary NRTIs (d4T, ZDV, TDF and ABC)



3TC and FTC Share of Paediatric Secondary NRTIs



Paediatric Share of NNRTIs and PIs



Summary – Paediatric API Market

- As a result of rapid scale up of PMTCT there are uncertainties in projecting number of children living with HIV, nevertheless, the number of children on treatment is expected to continue to increase.
- The TWG expects there to be a rapid phase out of NVP as normative bodies and donors prioritize more efficacious products such as LPV/r and DTG
- Paediatric patients over 20kg are currently able to take DTG 50mg tablets, and those under 20kg will be able to take DTG once dosing is established and a suitable product comes to market

Volume of Demand for ARVs (Person-Years) based on Average Projection of Linear, Country Target and Fast Track

Historical (2017-2018) vs Projection (2019-2023)

Drug	2017	2018	2019	2020	2021	2022	2023
d4T	9,673	10,457	7,793	7,080	6,216	5,429	4,859
ZDV	2,868,987	2,790,130	2,221,928	1,845,773	1,445,303	1,143,367	678,275
TDF	12,998,559	15,690,998	19,374,320	21,277,385	22,475,124	21,231,520	19,651,045
ABC	595,094	601,109	679,582	791,559	834,057	788,653	786,512
TAF			*	*	361,639	1,925,321	3,847,199
3TC	12,342,677	13,016,149	15,897,648	18,643,222	19,537,213	18,885,649	18,127,601
FTC	3,653,639	4,188,137	4,005,909	2,432,344	2,195,738	2,587,261	3,184,847
NVP	3,157,785	2,977,353	2,145,164	1,531,463	973,155	584,121	322,016
EFV	14,095,091	14,277,897	13,730,445	10,738,206	9,112,091	7,993,671	6,874,855
DTG	253,184	1,449,296	5,505,548	10,285,336	12,938,670	14,187,960	15,232,704
LPV	1,141,412	1,290,051	1,488,604	1,574,218	1,534,260	1,596,358	1,586,375
ATV	302,784	417,507	565,481	643,650	636,307	707,804	739,371
DRV	0	30,212	157,465	342,646	562,788	914,592	964,606
RTV	1,444,196	1,737,770	2,211,549	2,560,513	2,733,354	3,218,755	3,290,352

*Zambia has started TAF/FTC/DTG in Mid 2019

UNAIDS World Health Organization Avenir Health

Thank you

Collaborative Registration Procedure Pilot (CRP-Lite)

WHO-FDA Collaboration

November 25, 2019

Topics for Today

- Background of FDA's PEPFAR program
- Background on WHO's Collaborative Registration Procedure (CRP)
- CRP-Lite Background and Goals
- CRP-Lite Implementation
- CRP-Lite Current Status and Evaluation Plans

Background: FDA/PEPFAR

- FDA reviews HIV drugs for use by PEPFAR in partner countries
- “Tentative approval” process is used for drugs that cannot be marketed in the U.S. but meet all of FDA’s safety, efficacy, and quality requirements
- Two types of drugs are made available through FDA:
  - Generic drugs – duplicates of drugs approved for use in the U.S. (e.g. tenofovir DF 300 mg)
  - New drugs – variations in formulations, strengths, or combinations of previously approved drugs – but those not available in the U.S. (e.g., TLD)
- FDA typically expedites review of PEPFAR applications

Background: WHO's Collaborative Registration Procedure

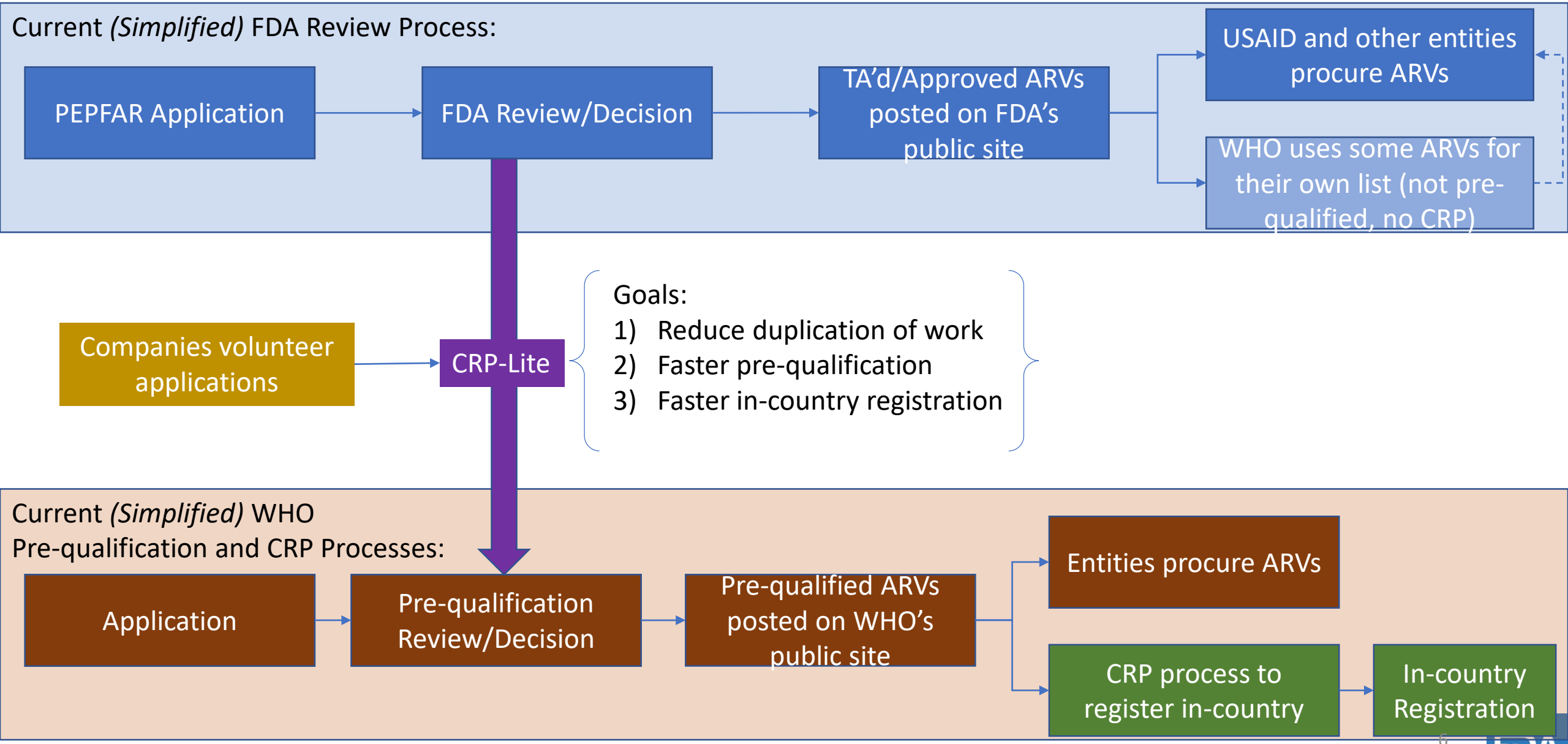
- WHO's CRP helps countries with developing regulatory systems to use WHO's own unredacted reviews to make decisions
- WHO Member States and companies opt-in to the process
- The drugs that go through CRP must be prequalified by WHO
- CRP is open to all drugs prequalified by WHO
- Countries that participate in CRP rely on WHO prequalification for initial registration and subsequent changes (supports life-cycle of the drug)
- Countries commit to making a decision on the drugs within 90 days

CRP-Lite Pilot

- The pilot will test whether FDA sharing of minimally redacted FDA reviews of PEPFAR products with WHO prequalification program will:
  - Reduce duplication of work between FDA and WHO
  - Speed up WHO's prequalification review process
  - Get the drugs registered faster in the countries that will ultimately use them via the CRP

- Potential for public health impact
  - Requested by WHO, Office of US Global AIDS Coordinator, and USAID
  - Requested at the Vatican meeting in 2017

How will CRP-Lite work?



CRP-Lite Coordination at FDA

- CRP-Lite Policy and Implementation Workgroup
  - Center for Drug Evaluation and Research (CDER):
    - Office of Generic Drugs/Policy
    - Office of New Drugs/Division of Antivirals
    - Office of Pharmaceutical Quality/OLDP
    - Office of Pharmaceutical Quality /DNDPI
    - Division of Information Disclosure Policy
    - Office of the Center Director
  - Office of Chief Counsel
  - Office of Global Policy and Strategy
  - Office of Public Health Strategy and Analysis – coordinator

FDA's Contributions and Roles

1. Coordinate with interested drug companies to get necessary permissions to share confidential information

2. Provide WHO's prequalification program with FDA's minimally redacted or unredacted reviews

3. Answer WHO questions on FDA's reviews

4. For the pilot, potential for in-person guidance by FDA reviewers

Selection of drugs for CRP-Lite

- WHO and companies are in the driver's seat
- Only products that have been tentatively or fully approved by the FDA are eligible
- FDA can advise but will not select products to go through the process
- PEPFAR entities, WHO, and the companies are encouraged to work together to help prioritize and select drugs needed by clinical programs

Current Status: Progress thus far…

- FDA has shared unredacted reviews for two applications with WHO
  - Permissions needed from multiple companies for a single drug
    - Application owners, DMF owners, and for establishment inspection reports for analytical/clinical sites
  - One pediatric and one adult

- Included reviews for “drug master files” or DMFs
  - DMFs contain the recipe for how to make the active pharmaceutical ingredient
  - Shared with permissions from DMF owners
  - This was a first for the FDA; the Agency has not shared the DMFs reviews with external parties before

Pilot evaluation

- FDA, WHO, and the companies will evaluate the pilot
- Pilot Endpoint: when each of the two pilot drugs have been registered in at least one CRP-participating country
- Pilot Outcome Measures are under development

Questions?

FDA contact for CRP-Lite issues:

Harinder Chahal
Office of the Commissioner

FDACRPLite@fda.hhs.gov

The Case of a Fictional Drug

PRESENTED NOT TO PROVIDE AN ANSWER BUT TO ILLUSTRATE FDA'S THINKING.

George Lunn
Office of Pharmaceutical Quality

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Drugs are no different.


Patients expect safe and effective medicine with every dose they take.

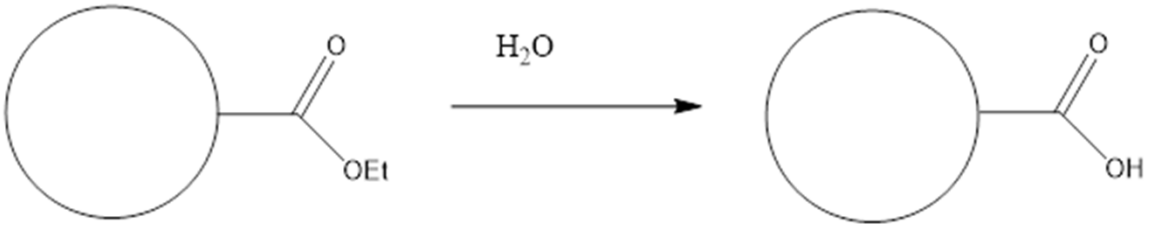
Pharmaceutical quality is

assuring *every* dose is safe and effective, free of contamination and defects.


It is what gives patients confidence
in their *next* dose of medicine.

Fictional Drug Example

"Nosuch" is an ester with the principle route of degradation being hydrolysis to the corresponding acid (Impurity A). Toxicological qualification provides an acceptance criterion of NMT 3.5% for Impurity A.



Nosuch

Nosuch acid
(Impurity A)

Using a Larger Bottle

- Up until now the drug has been marketed as a month's supply of 30 tablets in an HDPE bottle with an induction seal and desiccant.
- However, there is interest in dispensing more than one month at a time, so the applicant proposes a 180-day supply bottle.
- Because this drug product contains a hydrolytically unstable active we recommend an in-use stability study for 90-day or 180-day supplies. Similar recommendations might apply where the environmental conditions may impact stability, e.g., oxidative degradation, products containing amorphous dispersions.

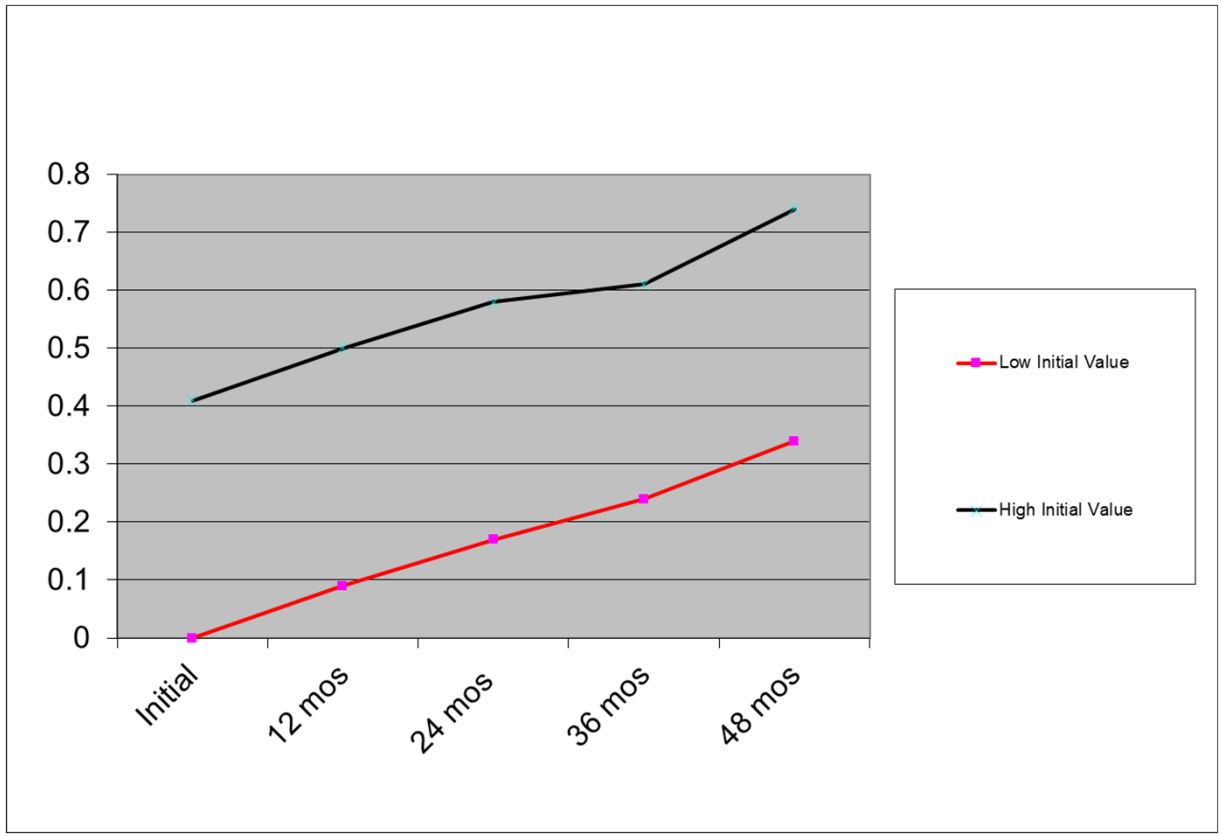
For a Solid Oral Dosage Form

It is common to observe a linear rate of degradation.

We have observed that product in different containers (30 vs. 180) may hydrolyze at different rates.

In Addition

We have observed that initial levels and increases during storage are often additive for solid oral dosage forms. Note how the curves are parallel.



So, for Solid Oral Products

- Degradation is often linear
- Degradation rate may depend on the container (e.g., amount of desiccant per tablet, desiccant:head space ratio)
- Degradants are “additive”

Returning to Our Fictional Drug

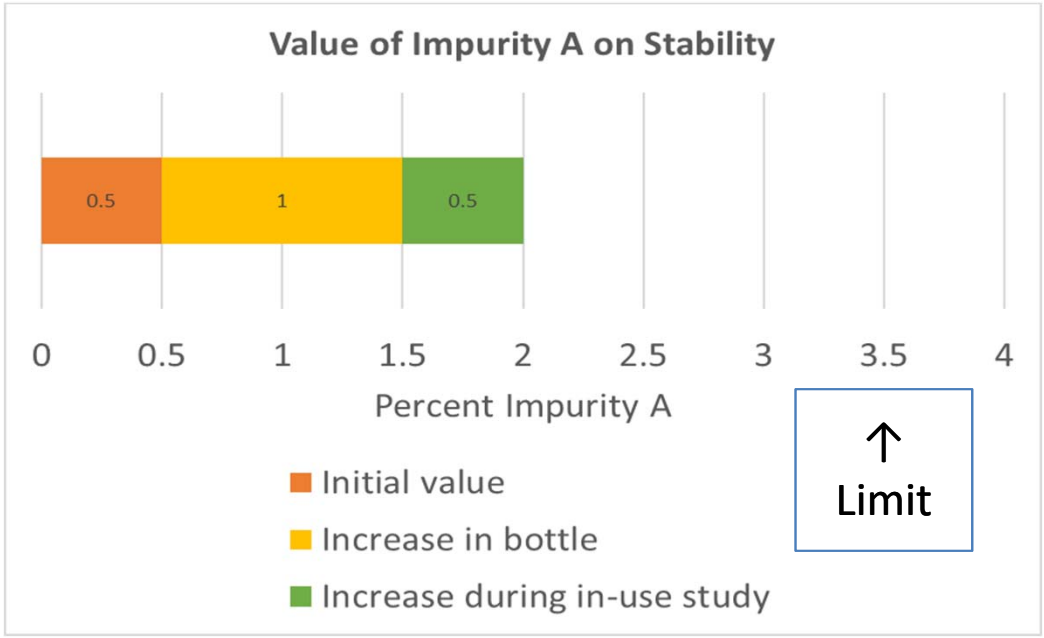
In order to maximize the expiration dating period consider three factors:

1. Levels of Impurity A at release
2. Increase during the long-term studies (in unopened bottle). Plan to include 36 and 48 month time points in the stability protocol
3. Increase during in-use study (because the API is sensitive to hydrolysis and a 180-day bottle is proposed)

The following slides will illustrate these points

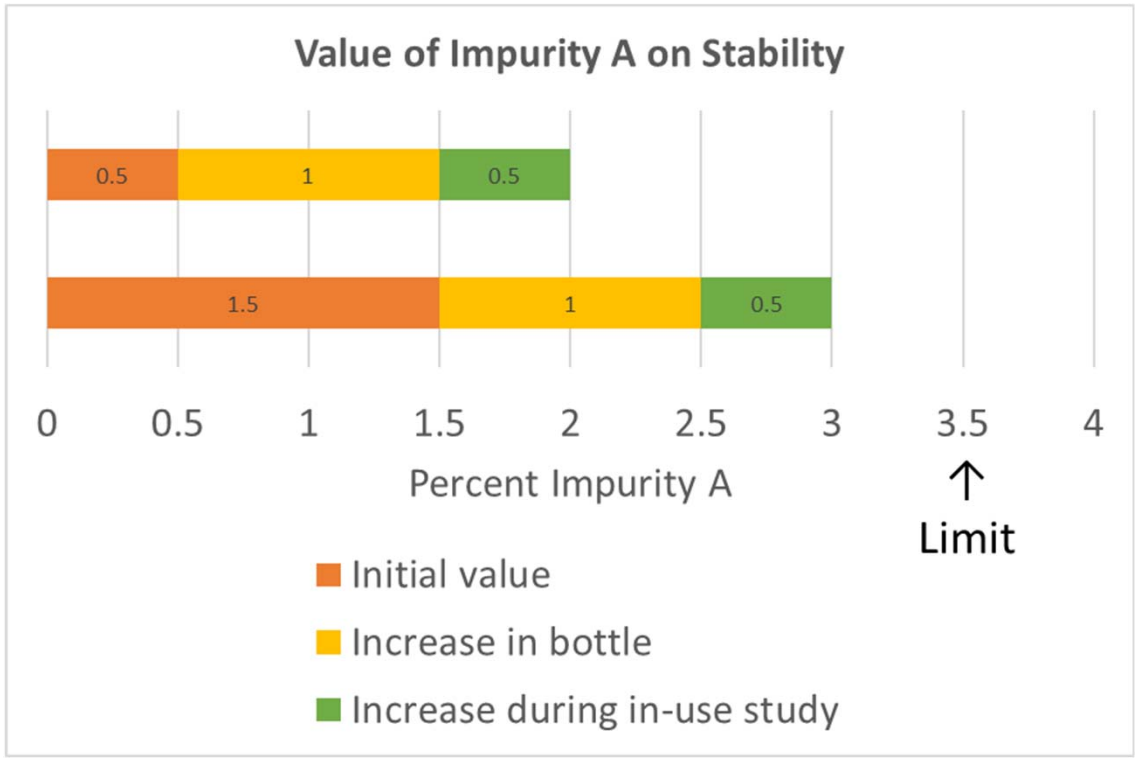
To maximize expiration dating period, consider 3 factors during design

- Initial level of degradant
- Increase of degradant during long-term studies of un-opened bottle
- Increase of degradant during in-use studies (for 90- or 180-count bottles)



The increase in the bottle is the predicted degradation over 24 months within an un-opened bottle; typically by extrapolation from 12 month data per ICH Q1E

Value of keeping release levels of the degradant as low as possible

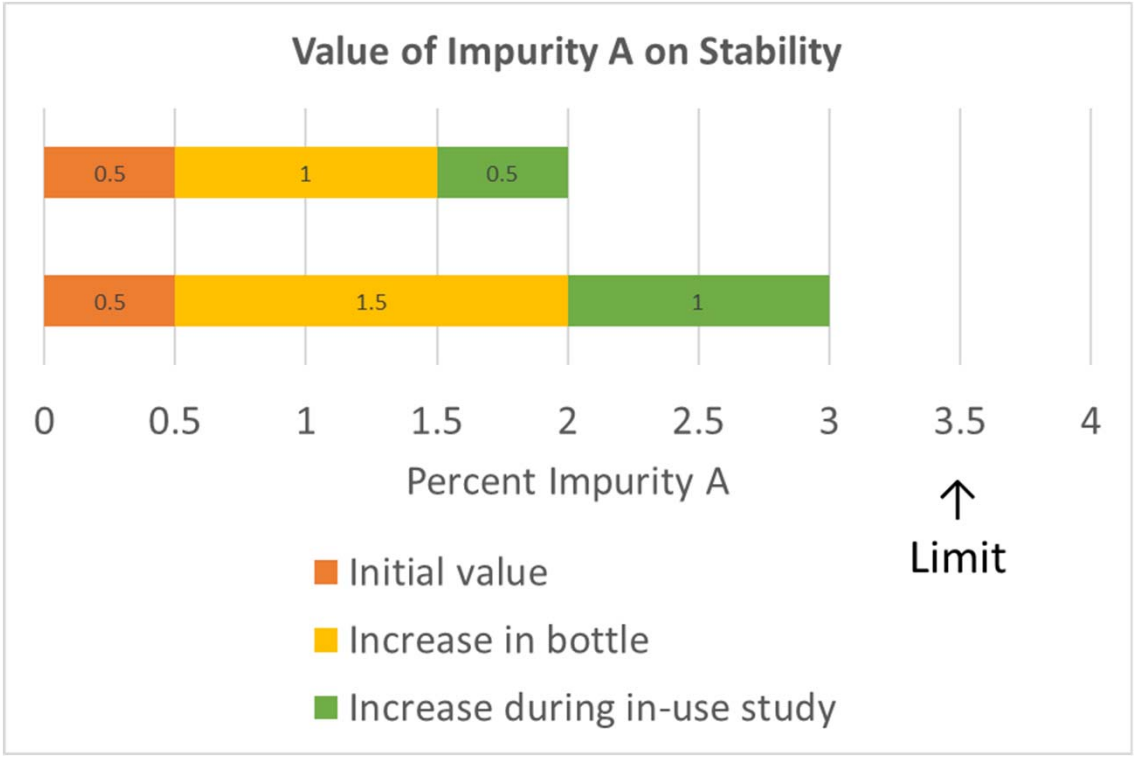


Product with low level of Imp A at release (top) might eventually be able to support 36 or 48 month expiry.

Explore In-Use for 90- or 180-day supply bottles, to guide design of the packaging

180 count, high desiccant→

180 count, low desiccant→



- Both packages can support an initial 24 month expiry period
- Applicant might commercialize the configuration with high desiccant load where eventual extension of expiry to 36 or 48 months might be possible.

Take Home Points

- Hydrolytic degradants should be kept as low as practical at release, perhaps with a tighter release specification
- Long-term stability studies (30°C/75% RH) could have 36 and 48 month time points planned so that the expiration dating period could eventually be extended
- Degradation of the product during repeated opening and closing of the bottle should be investigated for 90 and 180 day supplies of hydrolytically sensitive or amorphous products. This in-use study should be under reasonably realistic conditions.
  - Conduct in-use studies at 30°C/75% RH opening bottles every work day
  - Re-analyze tablets for in-use time = 0 if freshly made tablets are not used.

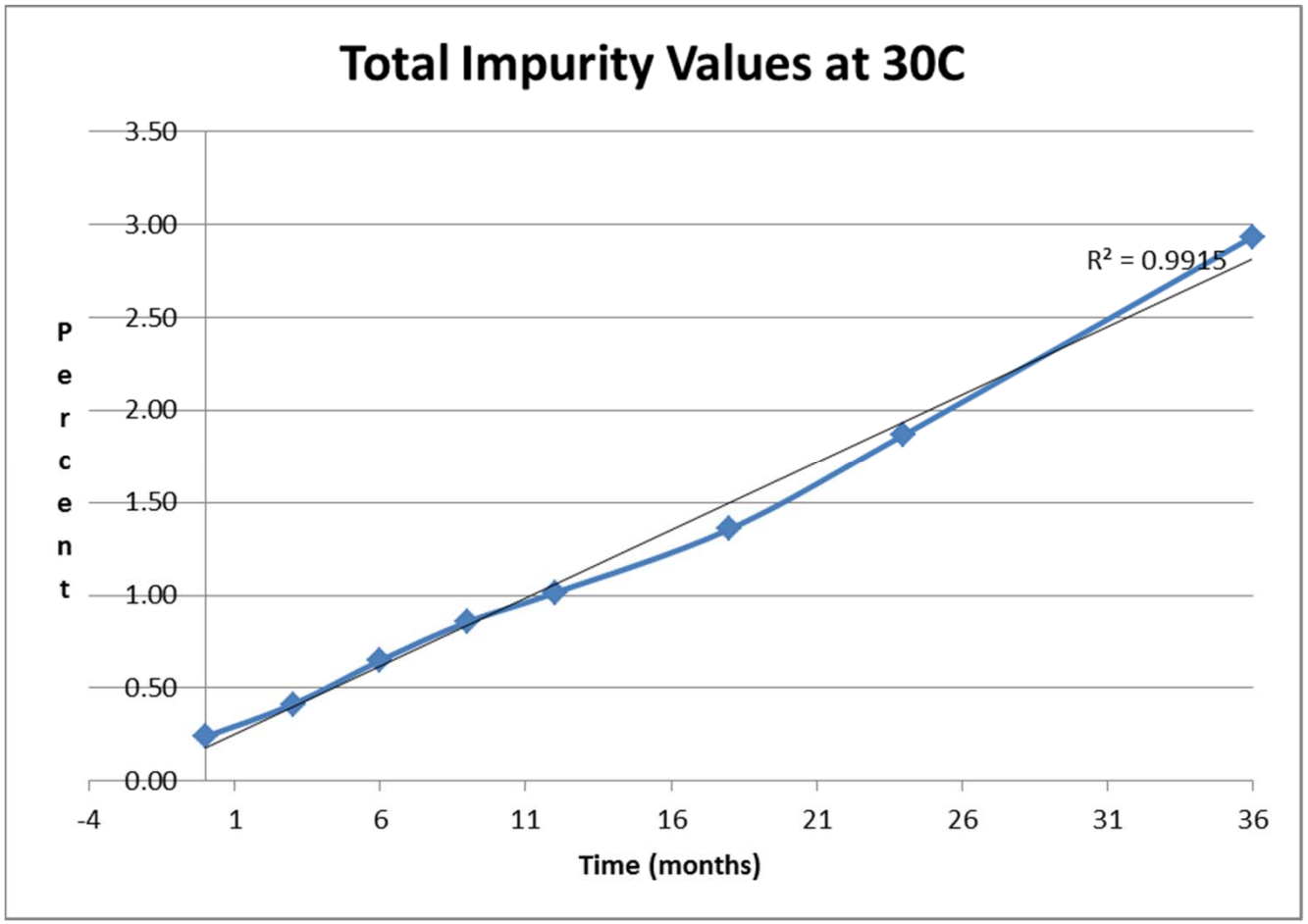
Thank You!

Back Up Slides

Suggestions for In-Use Studies

- Open bottle, remove induction seal and some amount of tablets (to increase head-space); use sufficient bottles for testing
- Leave desiccant(s) in the bottle (assuming that patients will be instructed “Do not remove desiccant”)
- Place reclosed bottle in 30°C/75%RH chamber
- Open bottle for several minutes within the chamber each work day and reclose
- Re-analyze tablets at time = 0 if freshly made tablets are not used
- At several time points including the final day (90th or 180th), remove sufficient tablets to perform analyses
- Attributes monitored would typically include assay, degradants, moisture content, and dissolution. Crystalline content would also be an important attribute for products containing amorphous active ingredient(s).

An example of linear degradation



Instructions for Pharmacists

Some concerns could be mitigated by adding instructions for pharmacists. For example here are some suggestions:

- Store and dispense in original bottle, protect from moisture, and keep bottle tightly closed. Do not remove desiccant
- Do not dispense if expiration date will be exceeded before the final tablet is consumed
  - Or, Dispense so that bottle(s) remain within expiration date at end of patient use
- Instruct patient to entirely consume one bottle before opening the second (if dispensing two 90 count bottles)

FDA Written Responses to Participants' Questions Submitted Through USAID for the 2019 Annual ARV Buyer Seller Summit – Washington, DC, USA

Questions received from Christine Malati (USAID) on October 15, 2019.

Q1. During the recent inspection of the API site of one of the API sources used in our submission USFDA has certain queries hence there was 483 issued by USFDA. To de risk we are planning to use an alternate source of the API and take the exhibit batches and submit it to USFDA. the questions are - 1) How many batches do we have to take, 2) Do we have to do the Bio equivalence study with this API source, 3) The stability data required would be for 3 months or 6 months? 4) the timelines for approval in this case? 5) Do we have to withdraw the dossier with the original source for fast tracking the approval with alternate source?

FDA Response to Q1: To obtain accurate and application-specific responses to these questions that may be sensitive or confidential, FDA encourages the applicant to contact the respective regulatory point of contacts listed below.

NDAs:	Monica Zeballos; Email: monica.zeballos@fda.hhs.gov
	David Araojo; Email: david.araojo@fda.hhs.gov
ANDAs:	The Regulatory Project Manager (RPM) assigned to the ANDA

In the meantime, below are examples of potential outcomes, with the assumption this is an original PEPFAR ANDA or PEPFAR NDA for an immediate release dosage form. However, these are very complex questions and, although certain broad principles can be applied, any answer to an individual case will be based on the facts specific to that case and will depend on many variables including but not limited to: drug product at issue, dosage form, inspectional findings, temporal or possible temporal relationship between variables, and facility history. Therefore, the two examples below, provided as Worse Case Scenario and Best Case Scenario should only be used as guidelines for applicants to understand potential outcomes.

Worse Case Scenario – Original active pharmaceutical ingredient (API) Supplier's 483 was *directly linked* to API used in the ANDA batches with concern as those listed in the guidance for industry *Alternate Source of the Active Pharmaceutical Ingredient in Pending ANDAs* (December 2000).

- The original API site would need to be withdrawn from the application and the new site added to the pending application. An evaluation of the new API manufacturing site would be initiated.
- Three new drug product exhibit batches would need to be made with at least two separate lots of API from the new API supplier and full stability including 6-month under both accelerated and long-term conditions (30°C/75%RH) would need to be submitted for the three new exhibit batches. For more information, see:

  - Guidance for industry *ANDA Submissions – Refuse-to-Receive Standards* (Rev. 2, December 2016);
  - Guidance for industry *Q1A(R2) Stability Testing of New Drug Substances and Products* (Rev. 2, November 2003);
  - Guidance for industry *ANDAs: Stability Testing of Drug Substances and Products, Q & A* (May 2014).
- If bioequivalence studies were needed to support the application, these would need to be repeated with the drug product made using the new API source.
- For both NDAs and ANDAs, dissolution profiles for the exhibit batches of drug product made from the new API source would be provided to support the proposed dissolution method and acceptance criteria. For ANDAs, dissolution profiles of the reference listed drug (RLD) should also be included in the application.

Best Case Scenario – Original API Supplier's 483 was unrelated to the API used in the ANDA batches and new supplier's API is equivalent to the original API with respect to the impurity profile and physical properties. See the draft guidance for industry *Postapproval Changes to Drug Substances* (published for comments Sept 2018)

- The original API site would need to be withdrawn from the application and the new site added to the pending application. An evaluation of the new API manufacturing site would be initiated.
- At least one drug product exhibit batch should be manufactured with the API from the new source; include in the submission at least 3 months of long-term and accelerated stability from an on-going study; also include a comparison to a drug product batch made from the original API (biobatch, if available) by dissolution profiles (multiple timepoints for each active ingredient using an appropriate dissolution method).
- Comparative drug substance data from the new API source for three pilot or larger scale batches would be needed vs. the original API source.
- Drug product stability studies for the original source would need to remain in place until the proposed end of shelf life.

Other Factors - The Following are examples of more complex situations that may impact potential outcomes:

- Significant differences in particle size or solid-state form between the API from the original source and the new API source.
- Observations on original API supplier's 483 fall between the Best Case Scenario and the Worst Case Scenario; in this situation the applicant's justification for data package to support new API source is an important part of the communication.
- For modified-release dosage forms, where more extensive data may be needed.

Timelines for Regulatory Action: For original NDAs, the submission of a new API manufacturing site, a significant amount of new information, or a new study to a pending application is usually considered a major amendment. A major amendment will extend the initial Prescription Drug User Fee Act (PDUFA) goal date by 3 months to provide time for a full

review of the submission. FDA will notify the applicant that a major amendment will be reviewed and the new PDUFA goal date. The review team decides whether to extend the initial PDUFA goal date and review the major amendment or defer review of it until a subsequent review cycle without extending the review clock.

For original ANDAs, submission of a new API manufacturing site would also be considered a major amendment. Review timeframes for Major Amendments can be found in the GDUFA II Commitment Letter. ANDAs submitted under the PEPFAR program may receive a priority review, which means that major amendment may receive a goal date between 6 and 10 months from the date of submission. Note that FDA will not prioritize an ANDA if the submission involves facilities that are subject to a recommendation of Official Action Indicated, except in certain cases in which it is determined that the submission must be prioritized to address a public health concern (see MAPP 5240.3 Rev. 4 Prioritization of the Review of Original ANDAs, Amendments, and Supplements).

Additional Note: A related situation is the addition of a second API source when there is no concern with the original API source. This is often submitted as a post-tentatively approved amendment for an ANDA/NDA. Typically, the information to support the additional API source would follow the recommendations in the Best Case Scenario, above, except that the original API manufacturing site would not be removed from the application.

Q2. How can the USG appropriately use this summit as an opportunity to impress upon the TLD sellers the critical need to conduct longer shelf-life stability studies for submission to USFDA for longer shelf life approval?

FDA Response to Q2: Because longer expiration dating periods are valuable for getting PEPFAR drugs to patients, FDA would like to clarify the approaches that we recommend for extending the expiration dating period. At the time the original PEPFAR application receives Tentative Approval, applicants will often have enough stability data to support a 24-month expiry period. This will typically be 12 or 18 months of long-term stability data at 30°C/75%RH plus 6 months of accelerated data at 40°C/75%RH. Applicants can follow the ICH guidance *Q1E Evaluation of Stability Data* when proposing to extrapolate the existing data to support a 24-month expiry period.

At some time after receiving Tentative Approval, the applicant will have collected 24 months of long-term stability data on the original 3 registration batches. At that time, the applicant may submit a PEPFAR Major ANDA Amendment for ANDAs or a PEPFAR Major Change Amendment for NDAs proposing to extend the expiration dating period for the drug product on the basis of real-time data plus extrapolation using acceptable statistical methods (i.e., the ICH Q1E approaches). For example, by extrapolating to a 36-month expiration dating period based on statistical analysis of 24-month stability data.

Alternatively, if the applicant does not believe that extrapolation is warranted, the applicant may wait until 36 months of stability data are available and then submit a PEPFAR Minor ANDA

Amendment for ANDAs or a PEPFAR Minor Change Amendment for NDAs proposing to extend the expiration dating period to 36 months. The review of chemistry and manufacturing amendments to a tentatively approved NDAs will be approached in a similar manner as supplements to approved NDAs; however, applicants can inquire with the Office of Pharmaceutical Quality (OPQ) for projected review timelines for their specific amendments. Refer to Table 1 for FDA review performance goals for ANDA amendments to tentatively approved ANDAs.

If supported by the stability data, further extension may be possible (e.g., 48 months, etc.) using either of the approaches outlined above.

Table 1. Review Performance Goals for ANDA Amendments

Submission Type	Goal
Standard Major ANDA Amendments	90% within 8 months of submission date if preapproval inspection not required.
	90% within 10 months of submission date if preapproval inspection required.
Priority Major ANDA Amendments	90% within 6 months of submission date if preapproval inspection not required.
	90% within 8 months of submission date if preapproval inspection required and applicant meets requirements under I(A)(4)(b).
	90% within 10 months of submission date if preapproval inspection required and applicant does not meet requirements as described under I(A)(4)(c).
Standard and Priority Minor ANDA Amendments	90% within 3 months of submission date.

Q3. faster approval available for ARV drugs?

FDA Response to Q3: All drug products tentatively approved and approved by FDA under the PEPFAR program have been determined by the Agency to meet all required standards for safety, efficacy, and quality applicable to marketing in the United States. Original NDAs (that are not new molecular entities) are designated a Standard Review (10 month) or Priority Review (6 month). The review designation establishes the timeline, milestones, and goal date by which an NDA is reviewed under PDUFA performance goals per the 21st Century Review process. For NDAs, Priority Review and fast track designation are already available and are applicable for ARVs that are aligned with the needs of the PEPFAR program. Refer to guidance for industry *Expedited Programs for Serious Conditions – Drugs and Biologics*.

The first several versions of a fixed-combination product or pediatric formulation that are aligned with PEPFAR needs also may qualify for a Priority Review.

Original ANDAs submitted under the PEPFAR program are eligible for Priority Review. The applicants should request priority review by including the following bolded statement on their ANDA Cover Letter: "Priority Review Request-PEPFAR." Review goals under the Generic Drug User Fee Act (GDUFA) are clearly delineated in the GDUFA II Commitment letter. Original ANDAs will receive either a standard 10-month review goal or an 8-month review goal. In order to receive priority review with an 8-month goal date rather than a standard 10-month goal date, an applicant must submit a Pre-Submission Facility Correspondence (PFC) to the Agency not later than 60 days prior to the submission of the ANDA, which contains complete and accurate information regarding facilities involved in manufacturing processes and testing of the drug that is the subject of the application (see draft guidance for industry *ANDAs: Pre-Submission of Facility Information Related to Prioritized Generic Drug Applications (Pre-Submission Facility Correspondence)* (November 2017). If a PFC is not submitted or a submitted PFC does not meet the criteria as outlined in the guidance, the ANDA will receive a standard 10-month GDUFA goal date.

Q4. Explain the process for review and approval of peds and adolescent data to support newer optimal drugs and the associated timelines and key issues to be adhered to in order to expedite the review process.

FDA Response to Q4: For review designation and timelines for NDAs, see response to question 3. NDAs for innovative products (e.g., new dosage forms intended for pediatric and adolescent populations) may require more data to support the efficacy and safety of the products if a previous applicant has not already received approval for that active ingredient or population. For changes to a previously approved drug product, a 505(b)(2) NDA may rely on the Agency's findings of safety and effectiveness for the previously approved product coupled with the information needed to support the change from the approved product. Changes in previously approved ARV drug products may be supported by submitting appropriate exposure-response or clinical data. FDA encourages applicants to request specific feedback for innovative products through our Pre-IND Consultation Program found at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/Overview/default.htm.

Q5. Will USFDA provide PRIORITY REVIEW for all PEPFAR submission, irrespective of number of NDA submission? For example, if USFDA received 8 NDA for FDC molecule (A+Z) for PEPFAR market, will USFDA provide PRIORITY REVIEW(PR) to only first 5 NDA or will provide PR to all 8 NDA submission?

FDA Response to Q5: Currently not all PEPFAR NDAs are designated a Priority Review designation. The first several versions of a fixed-combination product or pediatric formulation

that are aligned with PEPFAR needs may qualify for a Priority Review. The exact number of priority reviews will be decided based on product and medical need.

Q6. If the company A submits the NDA application for FDC products 5 years later than other competitors (more than 3 companies received the tentative approval), will STILL the company A get PRIORITY REVIEW as per the FDA HIV guidance?

FDA Response to Q6: The NDA would likely be designated as Standard Review.

Q7. The application fee was waived for a company's PEFAR FDC product. After the patent is expired, will this company need to Pay NDA Fee along with FAR?

FDA Response to Q7: If an applicant is granted a user fee waiver for its PEPFAR NDA that is tentatively approved, regardless of the expiration of the patent/exclusivity protection for the reference product(s), the applicant will not be subject to an application fee. But the applicant should be aware that it may be subject to the program fees if it receives final approval subsequently. The applicant can consider requesting a waiver of those program fees if it believes it fits the criteria set forth in the guidance for industry *User Fee Waivers, Reductions, and Refund for Drug and Biological Products* or the draft guidance for industry *Prescription Drug User Fee Act Waivers for Fixed-Combination Antiretroviral Drugs for the President's Emergency Plan for AIDS Relief*.

Q8. What is the scope of the Mutual Recognition Agreement (MRA) between FDA and European Union?

FDA Response to Q8: The scope of the MRA can be found in Article 3. "Article 3 Scope:

1.The provisions of this Annex apply to pharmaceutical inspections of manufacturing facilities carried out in the territory of a Party during the marketing of products (hereafter referred to as "post-approval inspections") and, to the extent provided for in Article 11, before products are marketed (hereafter referred to as "pre-approval inspections"), as well as, to the extent provided for in Article 8.3, to pharmaceutical inspections of manufacturing facilities carried out outside the territory of either Party.

2. Appendix 1 names the laws, regulations and administrative provisions governing these inspections and the GMPs requirements. 3. Appendix 2 lists all the authorities responsible for the oversight of facilities that manufacture products within the product coverage of this Annex. 4. Articles 6, 7, 8, 9, 10 and 11 of the Agreement do not apply to this Annex."

The MRA website can be found here: https://www.fda.gov/international-programs/international-arrangements/mutual-recognition-agreement-mra.

With the actual agreement included below:
https://ustr.gov/archive/assets/World_Regions/Europe_Middle_East/Europe/1998_US-EU_Mutual_Recognition_Agreement/asset_upload_file292_7083.pdf

Additional FAQ's document provided by USTR Office:
https://www.fda.gov/media/103391/download

Q9. Does all PEPFAR Tentatively Approved/Approved ARV (NDAs/ANDAs) published on Drugs@FDA website?

FDA Response to Q9: FDA's Drugs@FDA is a public database that allows users to search for official information (e.g., approval status, drug product labels, approval letters, reviews, approval history of a drug, etc.) about **FDA-approved** products. The official information is redacted to remove certain types of information such as trade secrets, confidential commercial information, and personal privacy information.

For tentatively approved PEPFAR ANDAs and NDAs, very limited information such as the **approval status** is published at Drugs@FDA. However, please refer to FDA's public website listed below that publishes tentatively approved/approved ARVs, both under ANDAs and NDAs, that are eligible for PEPFAR procurement.

Website: https://www.fda.gov/international-programs/presidents-emergency-plan-aids-relief-pepfar/tentatively-approved-and-approved-antiretrovirals-eligible-procurement-under-presidents-emergency.

Quality Assurance:
Expectations and Analyses

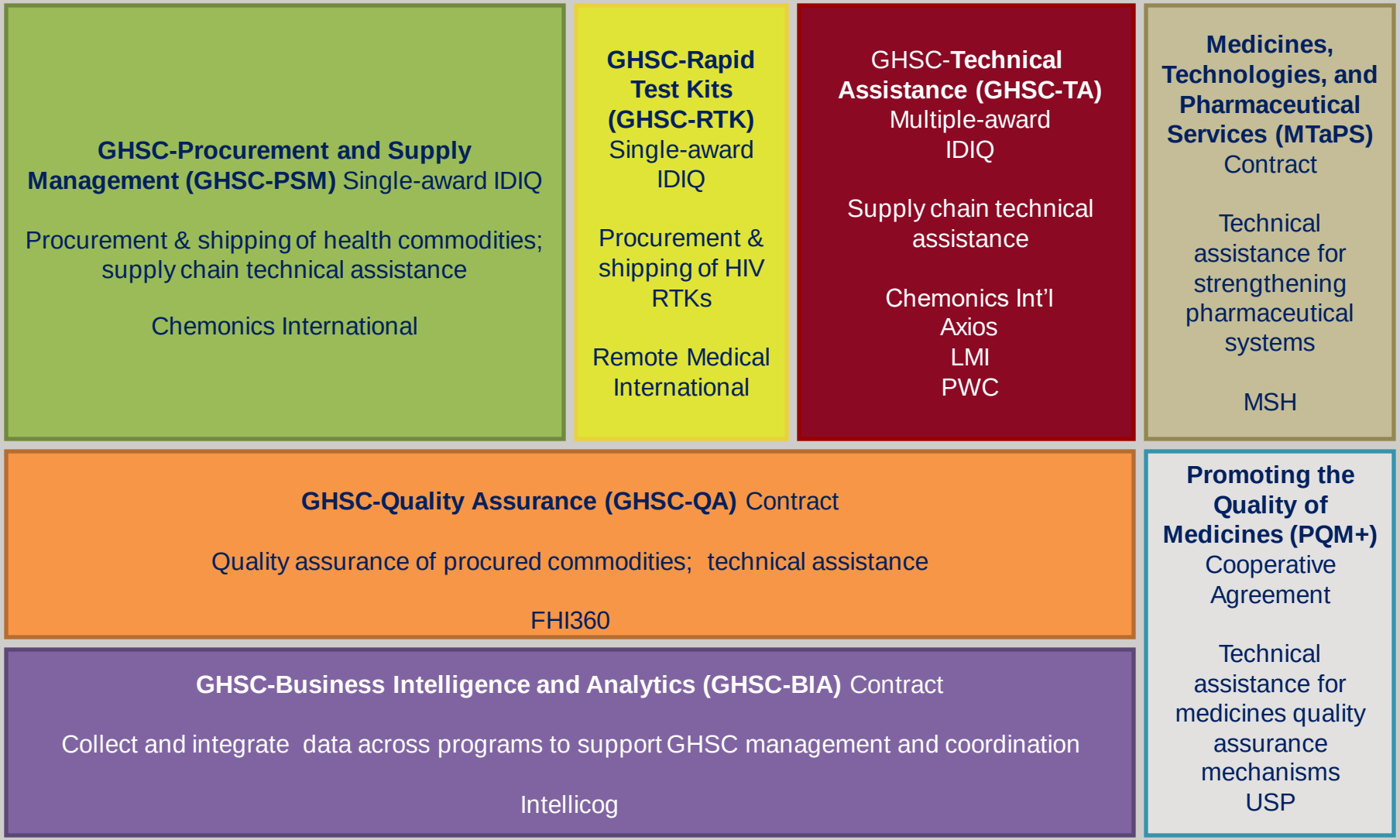
Christine Malati, USAID
Aida Cancel, fhi360
Hien Dinh, fhi360

2019 Annual ARV Buyer Seller Summit

Washington, DC, USA

November 25 – 27, 2019

USAID Global Health Supply Chain Program



Antiretrovirals Product Eligibility

- **USAID SCH.SOP.ARV-01.01**
  - USAID Antiretroviral Procurement Process (June 1, 2019)
    - Introduced to GHSC-PSM initially, followed by introductions with KEMSA and CDC MAUL

- Product Regulatory Status:
  - US FDA Approval OR Tentative Approval

Product Eligibility

- **Product Eligible List**
  - Active Ingredients
  - Strength
  - Dosage Form
  - Package Size
  - Shelf-life
  - Storage Conditions
  - Supplier
  - FPP Manufacturer
  - FPP Manufacturing Site(s)
  - Packaging Material
  - Regulatory Basis of Approval
  - US FDA Application Type and Number

https://www.ghsupplychain.org/for-suppliers/ghsc-eligible-lists

USAID Global Health Supply Chain Program

GHSC Eligible Lists

The USAID Global Health Supply Chain-Quality Assurance Program (GHSC-QA) maintains lists of products/suppliers that are eligible for procurement through the Global Health Supply Chain Program. Products and suppliers undergo a thorough technical review and must continue to meet quality standards to maintain eligibility for procurement.

Eligible lists include:

- Antiretrovirals
- Essential medicines
- Food by Prescription
- Gloves
- Male and Female Condoms and Personal Lubricants
- Voluntary Medical Male Circumcision Kits
- HIV Rapid Test Kits
- Reproductive Health Products
- Wholesalers

Product Eligibility

- **Product Information**
  - Collected through GHSC-QA Abbreviated Technical Product Questionnaire
  - Manufacturer provided documentation through RFQ manufacturing campaigns

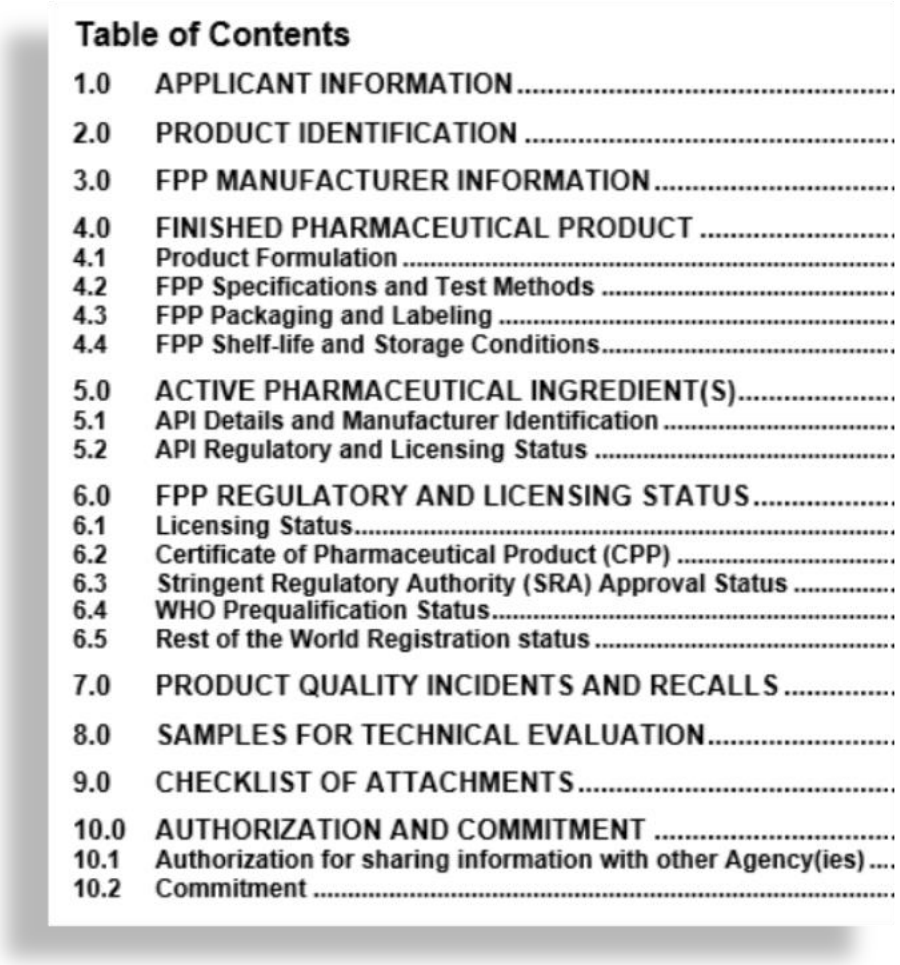


Table of Contents

Product Eligibility Challenges

- **Submission Challenges**
  - No Submission
  - Incomplete Documentation
  - Submitted old technical questionnaires, without updates. Thus detailed product information and updates are not available.

Product Eligibility Challenges

- **Eligibility Determination Challenges**
  - Not yet approved by US FDA (Under US FDA Assessment)
  - Discontinued US FDA application
  - Pack size submitted differs from US FDA approved pack size
  - Unable to validate FPP manufacturing site approval by US FDA
  - Unable to validate API manufacturing site approval by US FDA
  - Unable to validate that product meets requirements:
  - Shelf-life

Risk Evaluation

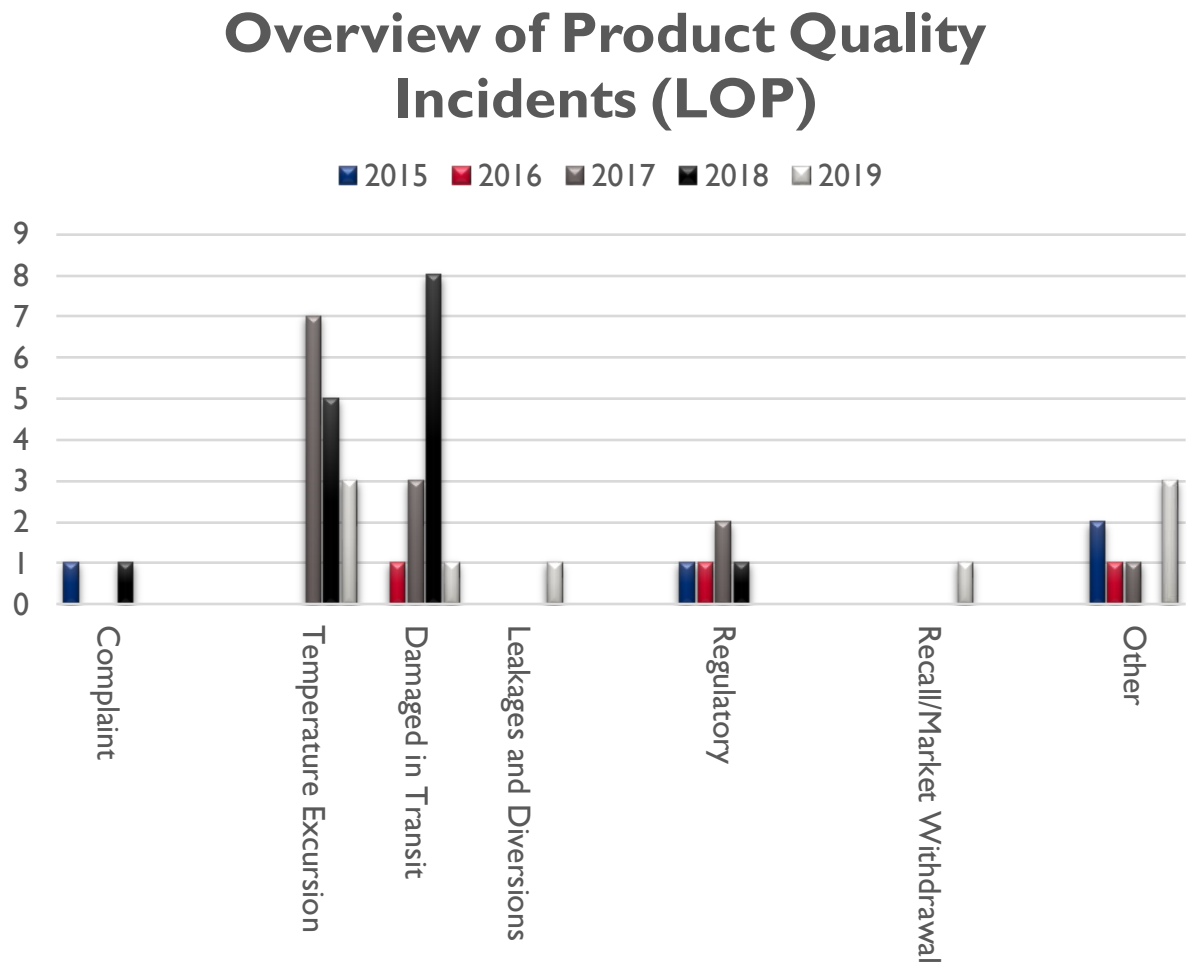
- **Evaluation Criteria**
  - FPP Manufacturing Site GMP Inspection
  - US FDA Warning Letters/Import Bans
  - Stability Data
  - API Manufacturing Site GMP Inspection
  - Package Insert/Patient Information Leaflet
  - Product Recall
  - Product Quality Incident: Out of Specifications
  - Product Release History (CpK)

Risk Evaluation

- **Summary**
  - Risks identified are mostly related to FPP and API manufacturing site GMP inspections.
  - 3 out of 22 FPP manufacturing sites with US FDA Official Action Indicated (OAI) classification which means regulatory and/or administrative actions are be recommended.
  - 14 APIs: 6 out of 29 API manufacturing sites reported with US FDA Official Action Indicated (OAI) classification

Product Quality Incidents

- **Summary**
- 5446 Lots Procured (Jan 2015-Oct 2019)
- 44 Product Quality Incidents reported (Jan 2015-Oct 2019): 0.8%
- No Out Of Specifications Incidents (0%)
- 1 Voluntary Recall (2019): (11 lots, 0.2%)
- Most Product Quality Incidents are Supply Chain related
  - 15 Temperature Excursions
  - 13 Damaged in Transit



GHSC-QA Summary

- Antiretrovirals are US FDA approved and continue to be a category of low risk to product quality.

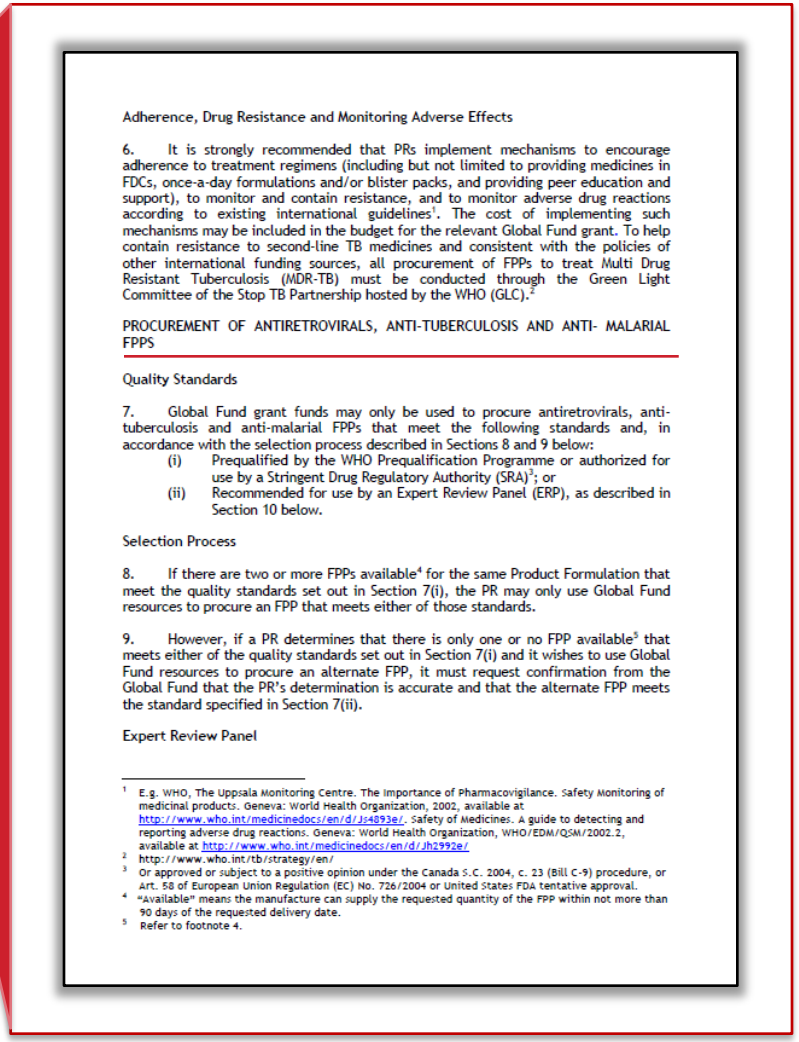
- GHSC-QA activities to obtain detailed product information and the continued communication with suppliers assists in updating the ARV eligible list with accurate information.

Global Fund Quality Assurance Policy

GLOBAL FUND QUALITY ASSURANCE POLICY FOR PHARMACEUTICAL PRODUCTS (as amended and restated on 14 December 2010

BASIC PRINCIPLE

1. Global Fund grant funds may only be used to procure finished pharmaceutical products (FPP) in accordance with the standards prescribed in this policy.



Adherence, Drug Resistance and Monitoring Adverse Effects

6. It is strongly recommended that PRs implement mechanisms to encourage adherence to treatment regimens (including but not limited to providing medicines in FDCs, once-a-day formulations and/or blister packs, and providing peer education and support), to monitor and contain resistance, and to monitor adverse drug reactions according to existing international guidelines[1]. The cost of implementing such mechanisms may be included in the budget for the relevant Global Fund grant. To help contain resistance to second-line TB medicines and consistent with the policies of other international funding sources, all procurement of FPPs to treat Multi Drug Resistant Tuberculosis (MDR-TB) must be conducted through the Green Light Committee of the Stop TB Partnership hosted by the WHO (GLC).[2]

PROCUREMENT OF ANTIRETROVIRALS, ANTI-TUBERCULOSIS AND ANTI- MALARIAL FPPS

Quality Standards

7. Global Fund grant funds may only be used to procure antiretrovirals, anti-tuberculosis and anti-malarial FPPs that meet the following standards and, in accordance with the selection process described in Sections 8 and 9 below:
   (i) Prequalified by the WHO Prequalification Programme or authorized for use by a Stringent Drug Regulatory Authority (SRA)[3]; or
   (ii) Recommended for use by an Expert Review Panel (ERP), as described in Section 10 below.

Selection Process

8. If there are two or more FPPs available[4] for the same Product Formulation that meet the quality standards set out in Section 7(i), the PR may only use Global Fund resources to procure an FPP that meets either of those standards.

9. However, if a PR determines that there is only one or no FPP available[5] that meets either of the quality standards set out in Section 7(i) and it wishes to use Global Fund resources to procure an alternate FPP, it must request confirmation from the Global Fund that the PR's determination is accurate and that the alternate FPP meets the standard specified in Section 7(ii).

Expert Review Panel

1 E.g. WHO, The Uppsala Monitoring Centre. The Importance of Pharmacovigilance. Safety Monitoring of medicinal products. Geneva: World Health Organization, 2002, available at http://www.who.int/medicinedocs/en/d/Js4893e/. Safety of Medicines. A guide to detecting and reporting adverse drug reactions. Geneva: World Health Organization, WHO/EDM/QSM/2002.2, available at http://www.who.int/medicinedocs/en/d/Jh2992e/

2 http://www.who.int/tb/strategy/en/

3 Or approved or subject to a positive opinion under the Canada S.C. 2004, c. 23 (Bill C-9) procedure, or Art. 58 of European Union Regulation (EC) No. 726/2004 or United States FDA tentative approval.

4 "Available" means the manufacture can supply the requested quantity of the FPP within not more than 90 days of the requested delivery date.

5 Refer to footnote 4.

Point of Contact:
Alain Prat | Team Leader, Quality Assurance
Alain.Prat@theglobalfund.org

More information: https://www.theglobalfund.org/en/sourcing-management/quality-assurance/

www.medicines4all.vcu.edu

Medicines for All

Improving Accessibility to Global Health Medicines

Eugene J. Choi, Ph.D.
Executive Director
Medicines for All Institute

Annual ARV Buyer Seller Summit Schedule
November 26, 2019

Improving Access to Affordable Medicines

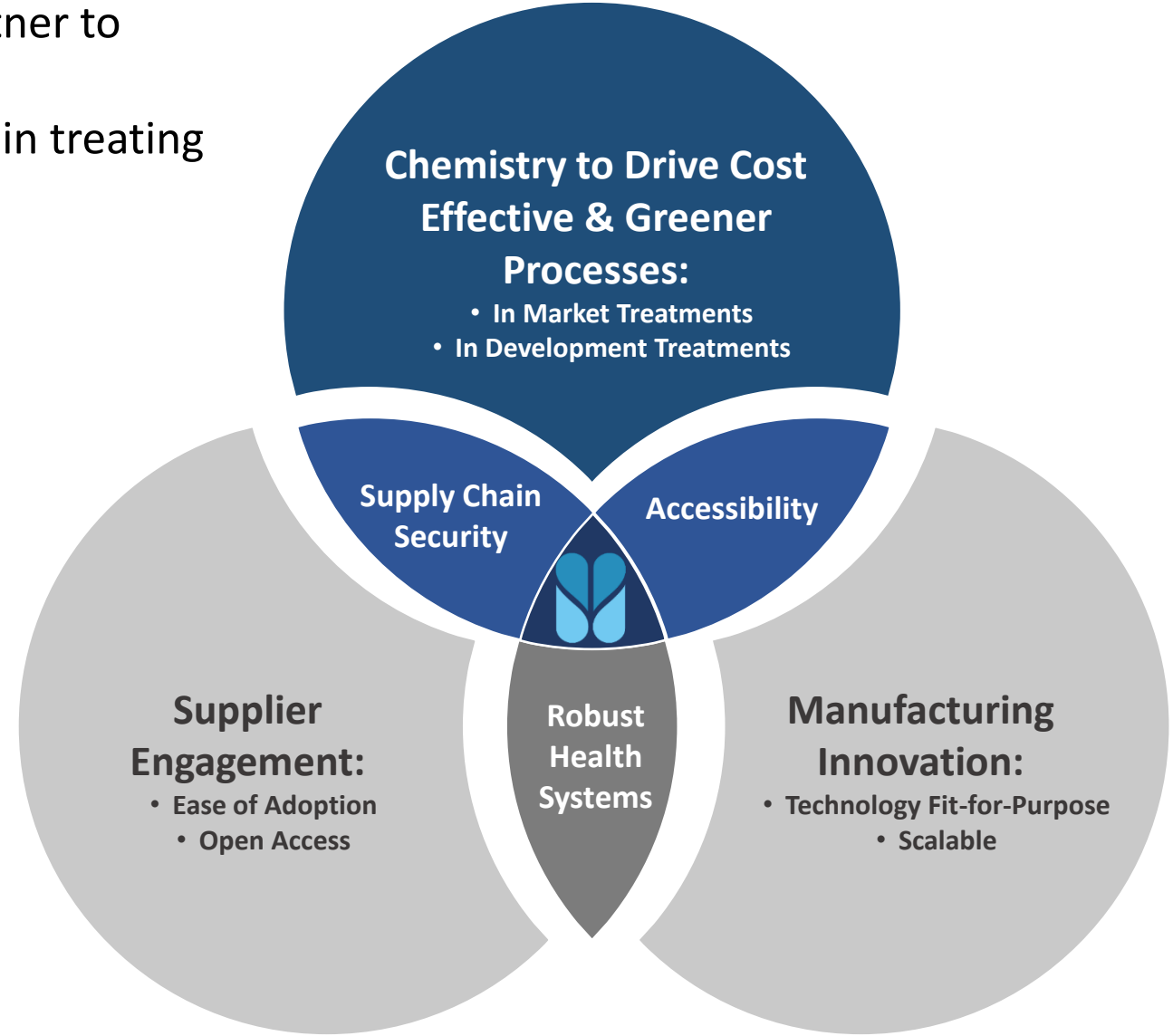
medicines for all institute

www.medicines4all.vcu.edu

The Medicines for All Institute (M4ALL) is a global partner to developers, manufacturers, and procurers of active pharmaceutical ingredients (APIs), a major cost driver in treating diseases around the world:

- Unconstrained academic ingenuity combined with pragmatic industrial applications experience
- Agile & innovative
- Demonstrated experience facilitating engagement across the entire product life cycle for global health medications
- Quantifiable outcomes in the marketplace and to patients

We offer de-risking solutions for all stakeholders, including procurers & manufacturers



Overview

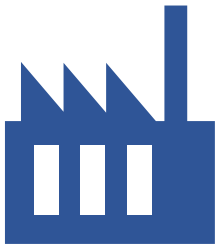
www.medicines4all.vcu.edu

- **Medicines For All Institute:** Established in July 2017 within the Virginia Commonwealth University College of Engineering with funding from the Bill & Melinda Gates Foundation.
- **M4ALL Capabilities:** M4ALL has developed unique capabilities and techniques to:
  - Reduce active pharmaceutical ingredient (API) costs,
  - Reduce the amount of waste generated in the manufacturing process, and
  - Reduce the number of unit operations and improve yields
- **M4ALL's Work To Date Has Shown:** even mature, aggressively procured, and aggressively optimized treatments can often be made both cheaper and greener.
- **M4ALL Value Proposition:** rapid, affordable, impactful (access-enhancing) optimization of treatments across disease states and treatments in market or in development.

Our Mission

www.medicines4all.vcu.edu

Improve Access to Safe, Effective and Affordable Medicines



Introduce new, easily transitioned routes to critical medicines

Develop new methods, technology and approaches

Train the next generation of process oriented innovators

Challenges in Global Health

medicines for all institute
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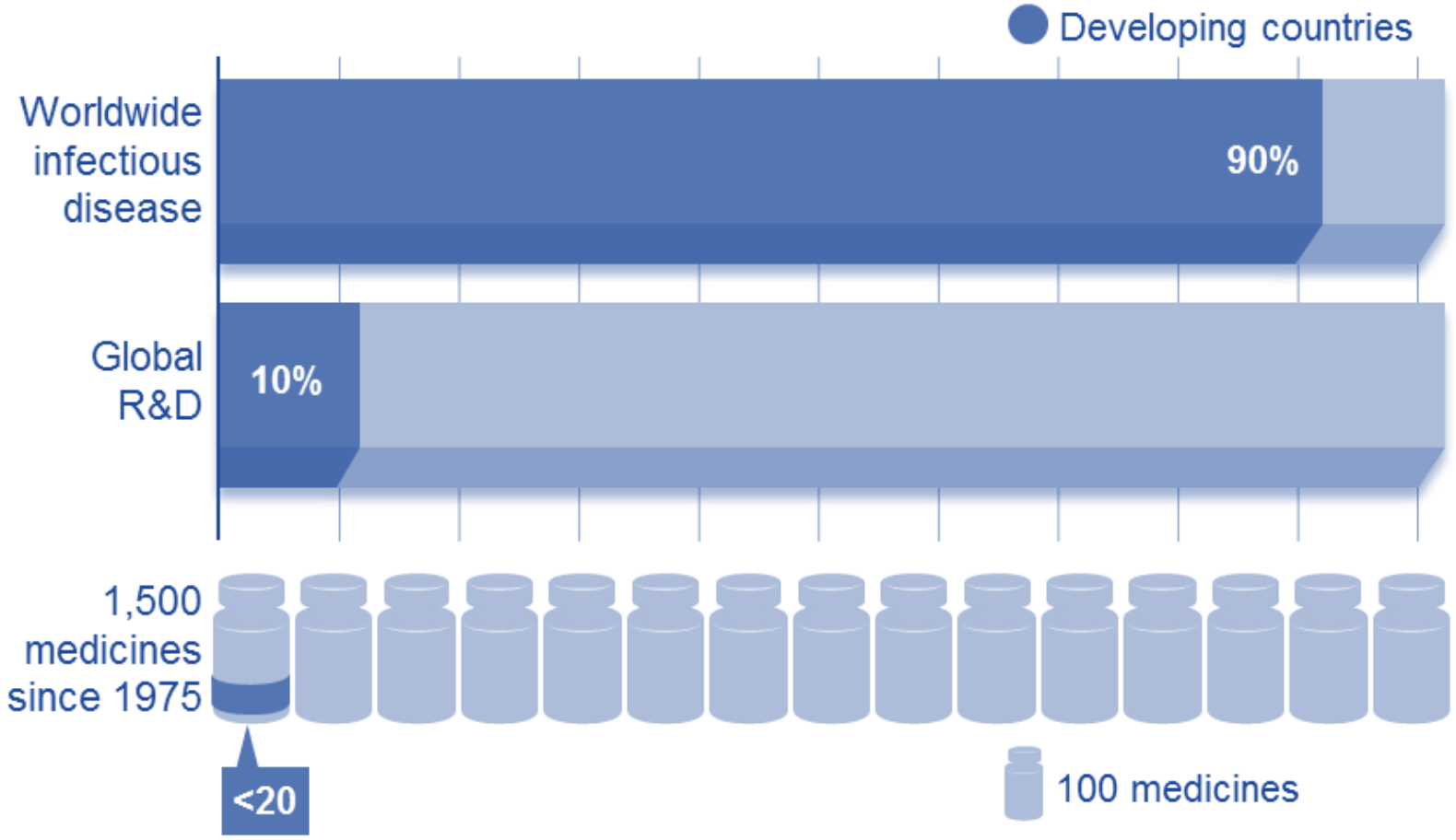
90% of the world's infectious disease burden is in developing countries.

10% of global R&D addresses developing countries' needs.

Fewer than 20 of the 1,500 medicines licensed since 1975 have been for diseases that primarily affect developing countries.



HIV Treatment Prices

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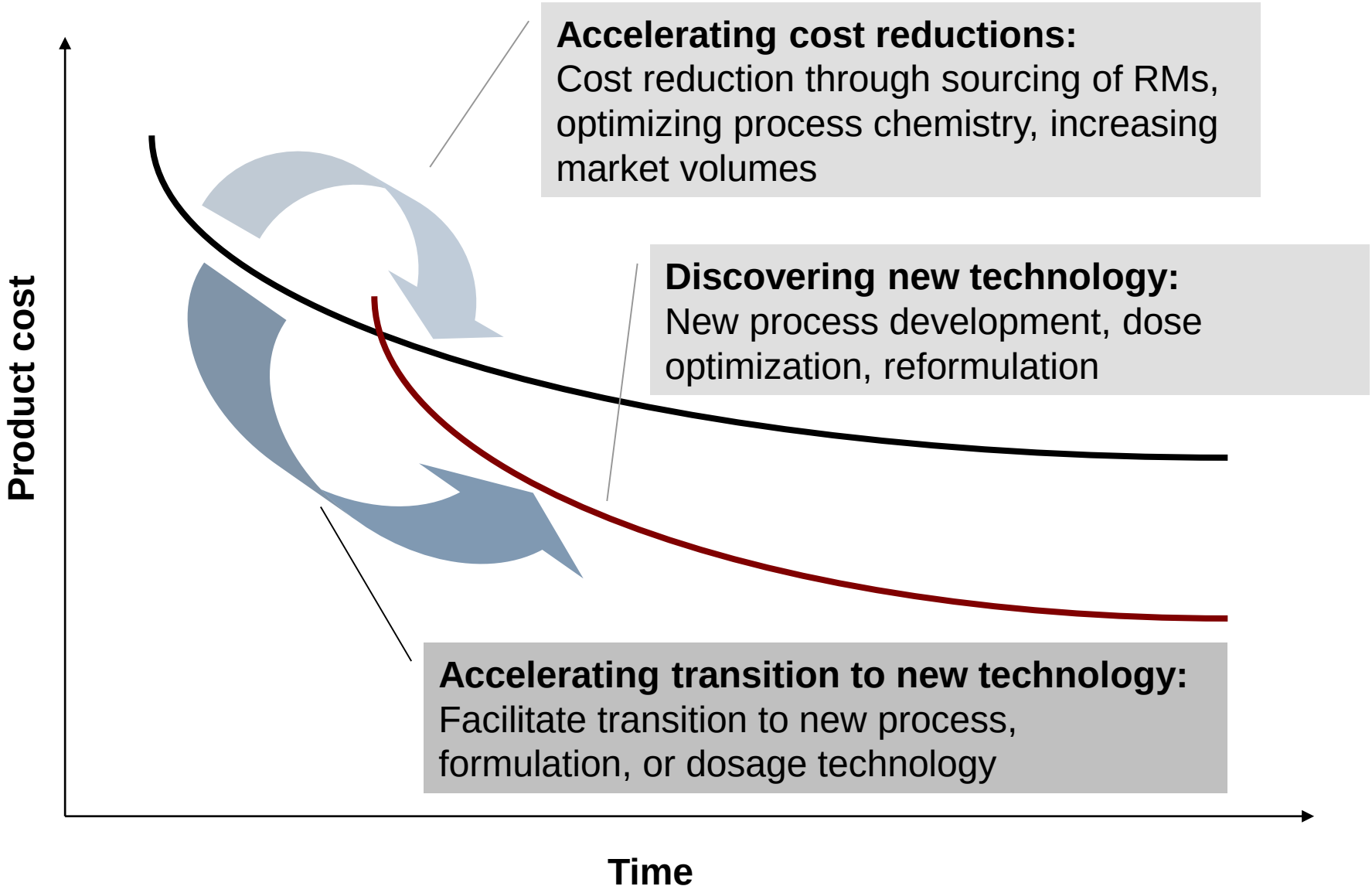

Accelerating cost reductions:
Cost reduction through sourcing of RMs, optimizing process chemistry, increasing market volumes

Discovering new technology:
New process development, dose optimization, reformulation

Accelerating transition to new technology:
Facilitate transition to new process, formulation, or dosage technology

State of Pharmaceutical Manufacturing

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Primary Cost Drivers in Today's Active Pharmaceutical Ingredient (API) Manufacturing

Complex, high cost **raw materials**, leading to high cost of goods (COGs) and constricted and/or unreliable supply

Needed: more extensive use of inexpensive starting materials

Very high **solvent consumption** and **waste**, leading to higher cost and environmental impact

Needed: fewer unit operations, higher overall yield, fewer solvent changes

Inflexible processing technologies and equipment trains that require high volumes to reach economies of scale

Needed: manufacturability in both batch and flow (lower capital costs, economies of scale at lower volumes)

M4ALL Approach

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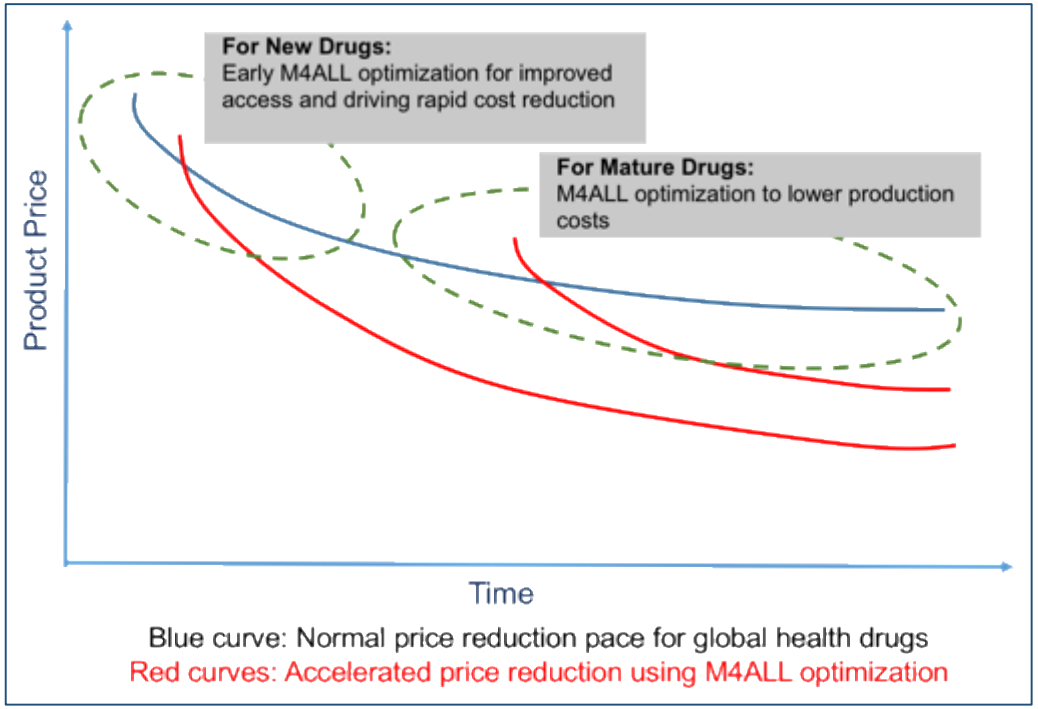
M4ALL Approach:

Building on our extensive molecular background, we are creating the global center of excellence that will drive increased access to pharmaceuticals

- New Synthetic Methods
- Novel Manufacturing Platforms
- Green Chemistry Approaches/Methodologies
- Effective Implementation and Uptake Strategies
- Drug Process Life Cycle Insights



M4ALL: Transforming Access To Both In Market and In Development Treatments

Our Building Blocks

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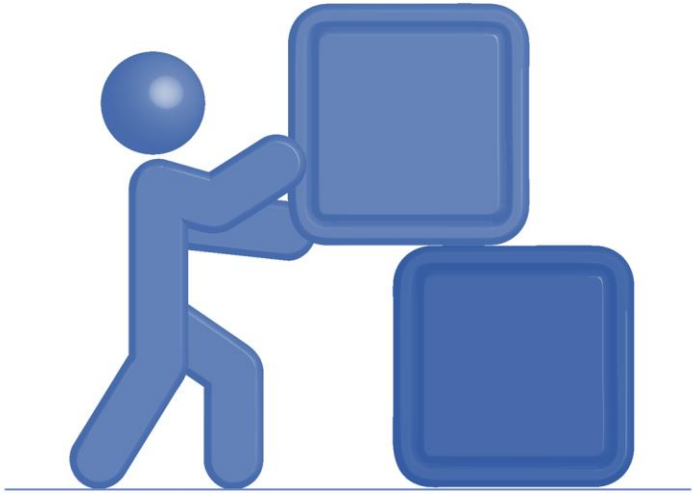
- Synthetic Chemistry
- Fitting Tools to Purpose
- Metrics Driven Process



Metrics Driven Process

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$

Process Cost of Goods

Σ starting material costs * Σ Yield

Process Mass Intensity

$$PMI = \frac{\text{mass of reactants}}{\text{mass of products}}$$

Environmental Policy Changes

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www.medicines4all.vcu.edu

- In 2017, the Chinese government initiated inspections of manufacturing facilities to root out air and water pollution
- By early 2018, nearly 40% of Chinese factories in 30 industrial provinces were interrupted (plant closings, fines, arrests)

Excerpt from a memo received by the Italian chemical company Amsa.

Credit: C&EN/Shutterstock

Approach: M4ALL Process Framework

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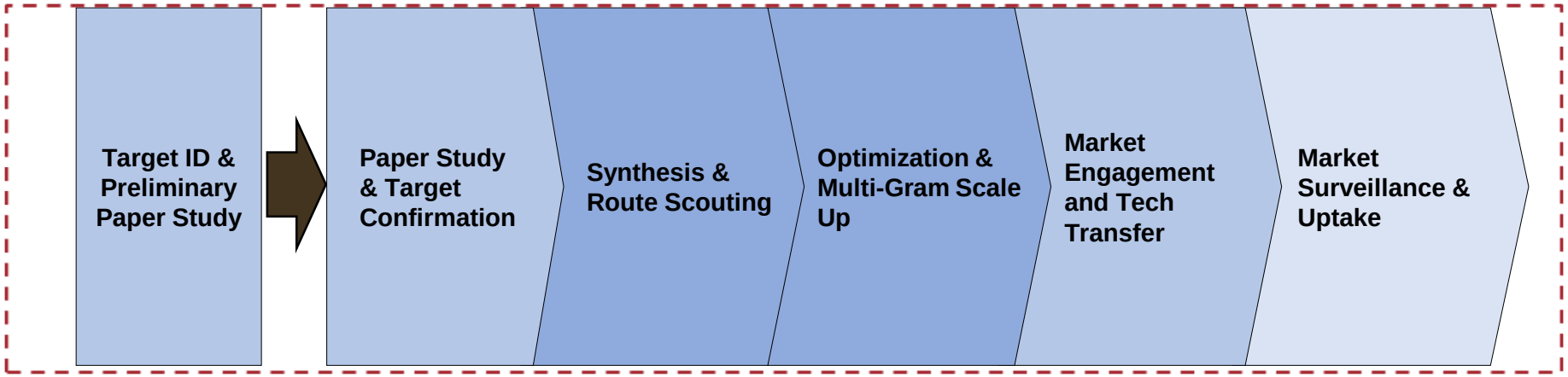
M4ALL focuses on the entire lifecycle of process development of critical APIs

M4ALL Process Phases



De-Risking Measures:

- Techno-Economic Analyses & Paper Studies to benchmark and develop novel strategies
- Route Scouting to demonstrate proof of concept
- Reproducibility & Scalability of processes to increase ease of implementation

Open Access Model for HIV Drugs

medicines for all institute

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1) M4ALL develops "Special Notice" public announcement inviting manufacturers to a workshop or webinar to presenting M4ALL's research

2) M4ALL posts Special Notice on its website & sends to its partners to distribute to their network of manufacturers

CLINTON HEALTH ACCESS INITIATIVE

medicines patent pool

USAID FROM THE AMERICAN PEOPLE

Chemonics Development works here

3) M4ALL conducts workshop or webinar presenting target research & follow-up discussions with manufacturers

4) M4ALL Process Development Report is posted on M4ALL's website & is sent to GH partners for distribution

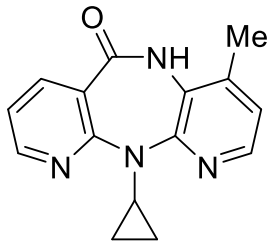
5) Under a non-exclusive basis, M4ALL helps manufacturers implement process(es)

Putting it Together: Nevirapine Example

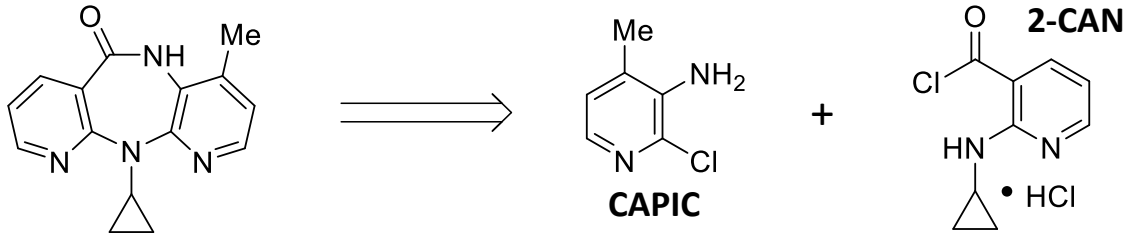
www.medicines4all.vcu.edu

Nevirapine:

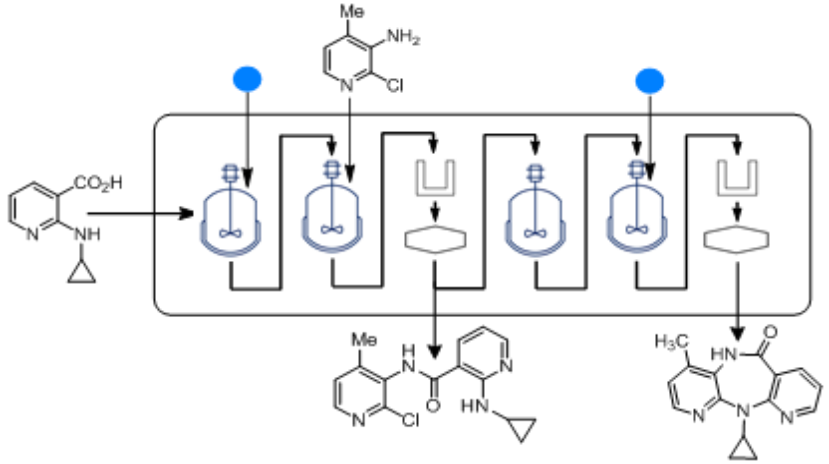
- Anti-HIV
- NNRT Inhibitor
- Innovator: BI



Current route uses the following registered starting materials.
The process has many unit operations, high PMI and costly starting materials:

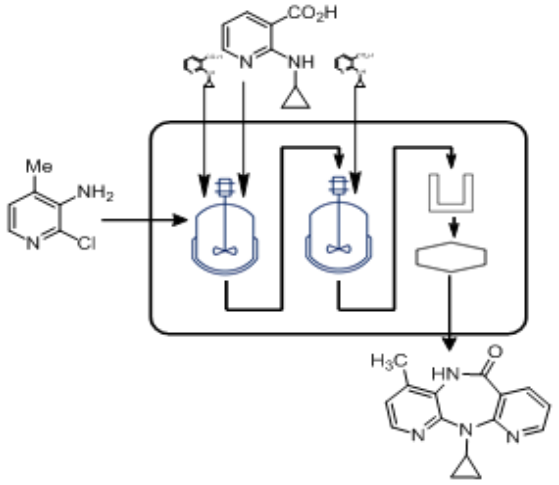


2nd Generation Nevirapine Process



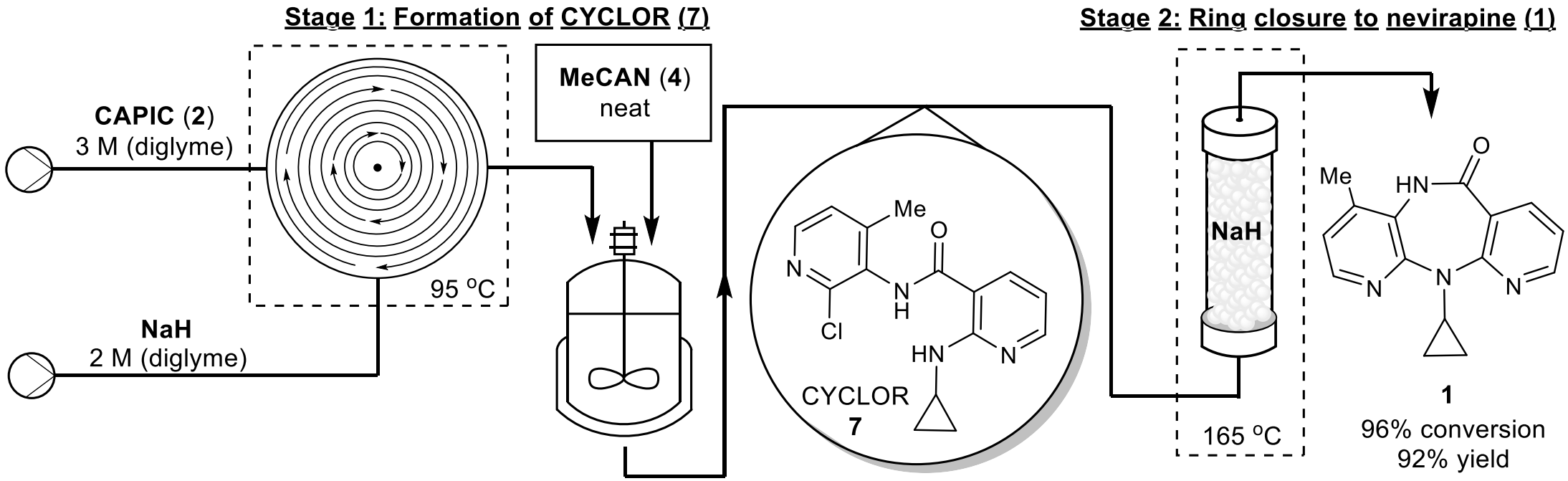
- Cost & PMI as driving metrics
- Seek routes starting from commodity raw materials
- Enumerate many possible approaches up front
- Avoid registered intermediate changes

M4ALL Nevirapine Process



Flow Chemistry for Nevirapine

Nevirapine



Vergese et al. *Green Chemistry* **2017**, *19*, 2986-2991.

Nevirapine: Full Roadmap

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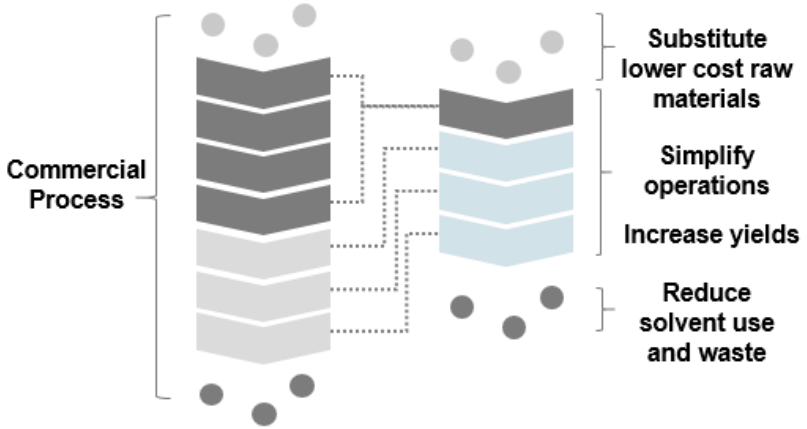
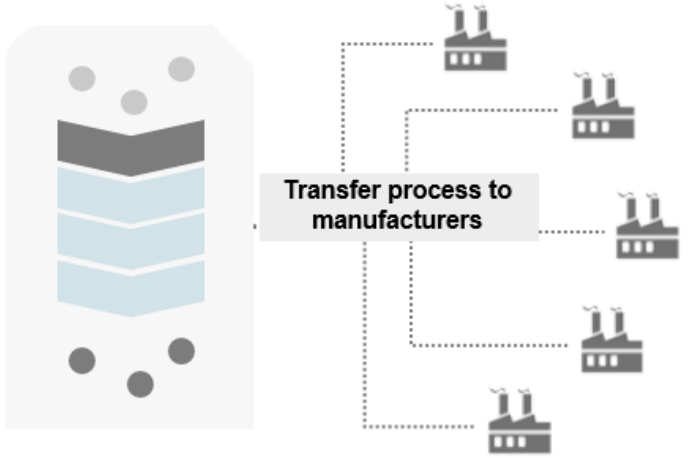
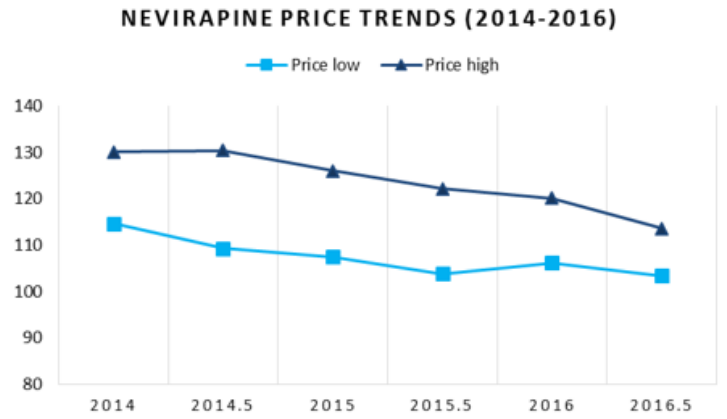
1 Novel Chemistry



2 Transfer to API Manufacturers



3 Track Price Reductions



NEVIRAPINE PROGRESS

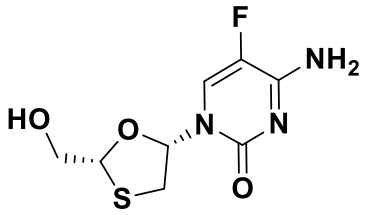
• 21 Unit Operations	• 11 Unit Operations
• 50% Isolated Yield	• 87% Isolated Yield
• Starting Material Cost: $100/kg	• Starting Material Cost: $60/kg
• Waste-to-drug mass: 80	• Waste-to-drug mass: 4

RESULTS: ≥30% lower COGs

- New process transferred to CHAI
- Both generic manufacturers in China have implemented the process

- Process established to monitor market price change
- 9% price decrease so far which translates to estimated savings of approximately $7.8M in 2015 alone

Emtricitabine (FTC) Example



Emtricitabine (FTC)

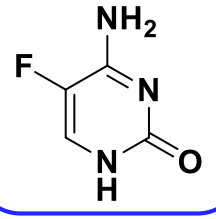
Volume sale: 120 MT/year

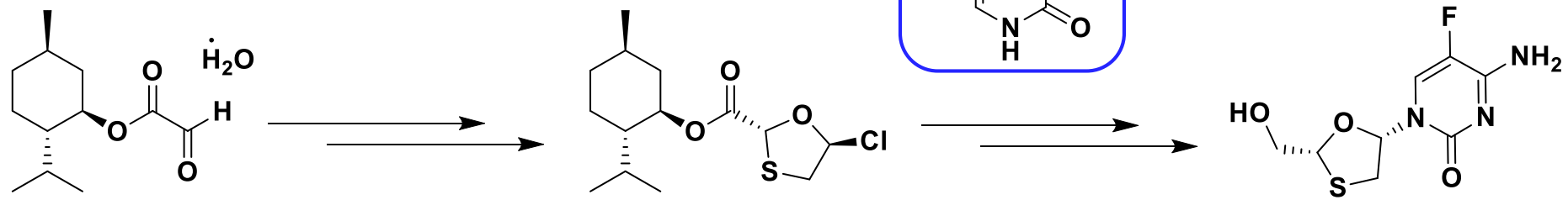
Anti-HIV

Emtriva™ (**FTC**)
Truvada™ (**FTC + TDF**)
Atripla™ (**TDF + FTC + EFV**)

Common Route for FTC

Cost Driver



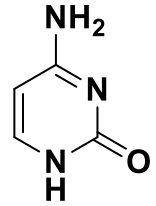


Pure FTC
30%
$307/kg

US Patent 8748604 B2 (2011)(Ranbaxy)

5-Fluorocytosine – Prices Rising

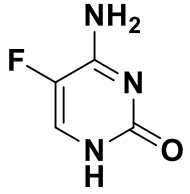
In December 2017, an explosion occurred at one of the largest manufacturers (Touxin Co in Xin Xiang province in China) of cytosine



cytosine

2016
$16/kg

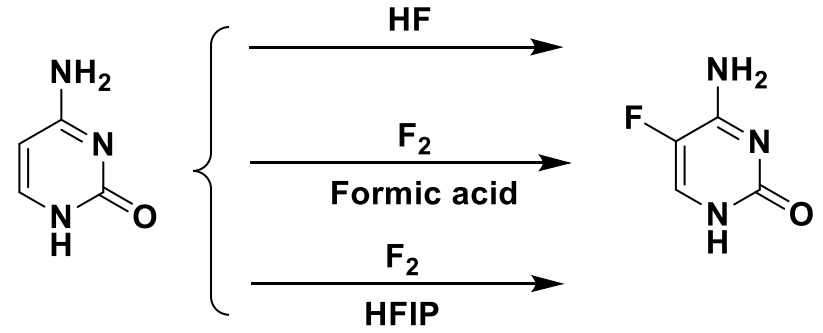
2018
$28/kg



5-fluorocytosine (5-FC)

2016
$32/kg

2018
$78/kg



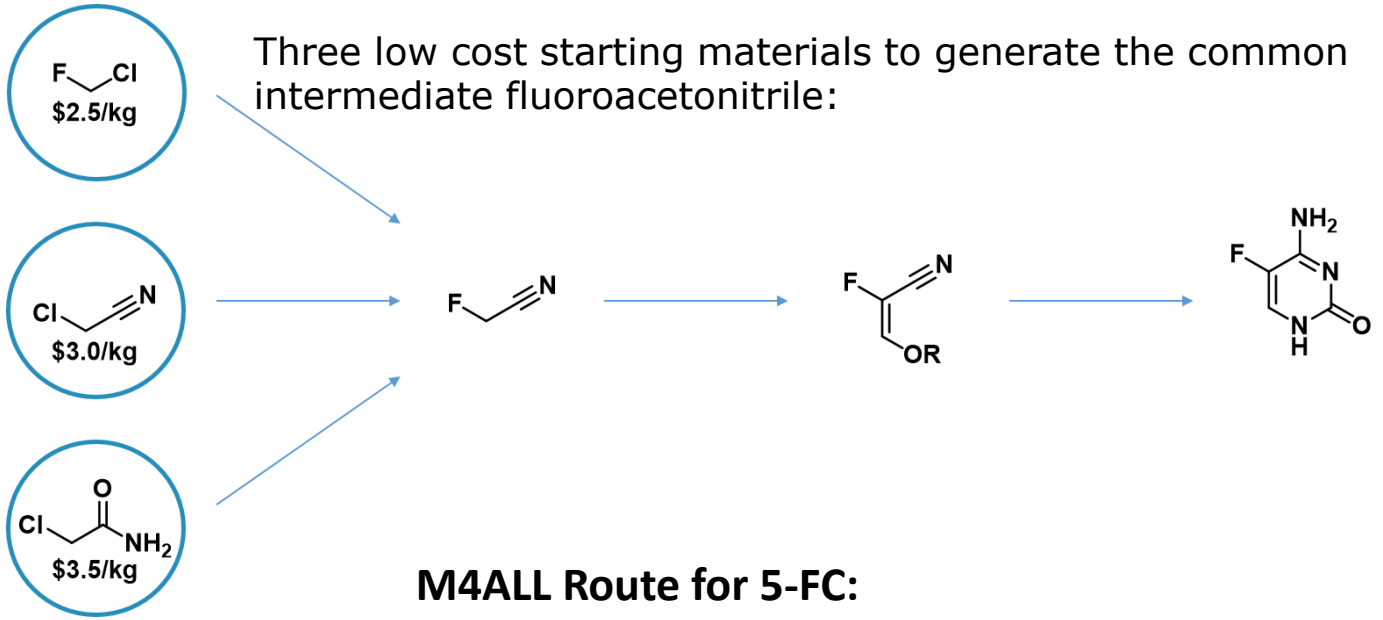
1. Toxic Reagents (HF, F_2)
2. Requires special permit
3. Reaction scale limited by regulation
4. Expensive installation of the Fluorine
5. Volatile cost of 5-FC

M4ALL Synthesis from Acyclic SMs

www.medicines4all.vcu.edu

Original Process Released Jan 2019

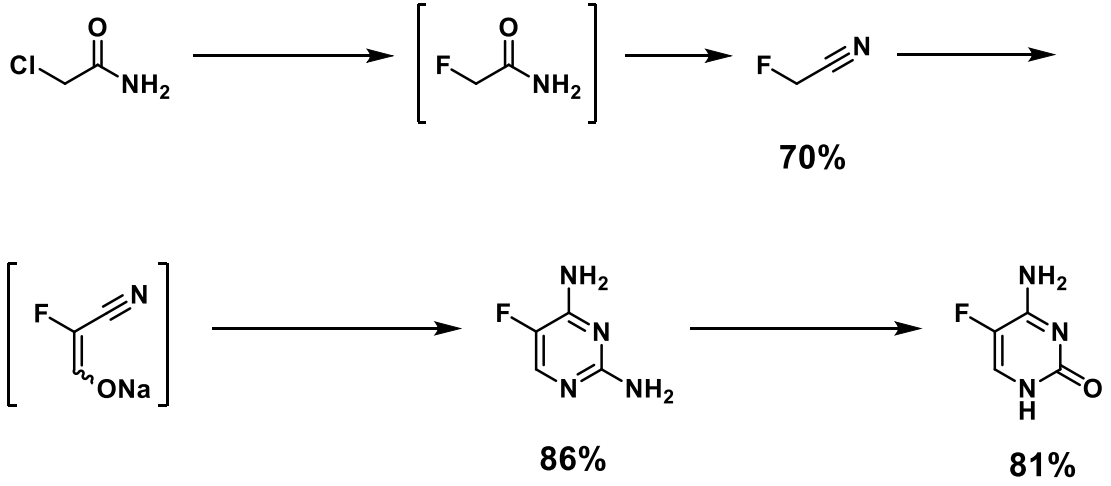
Updated Process Released Nov 2019



Three low cost starting materials to generate the common intermediate fluoroacetonitrile:

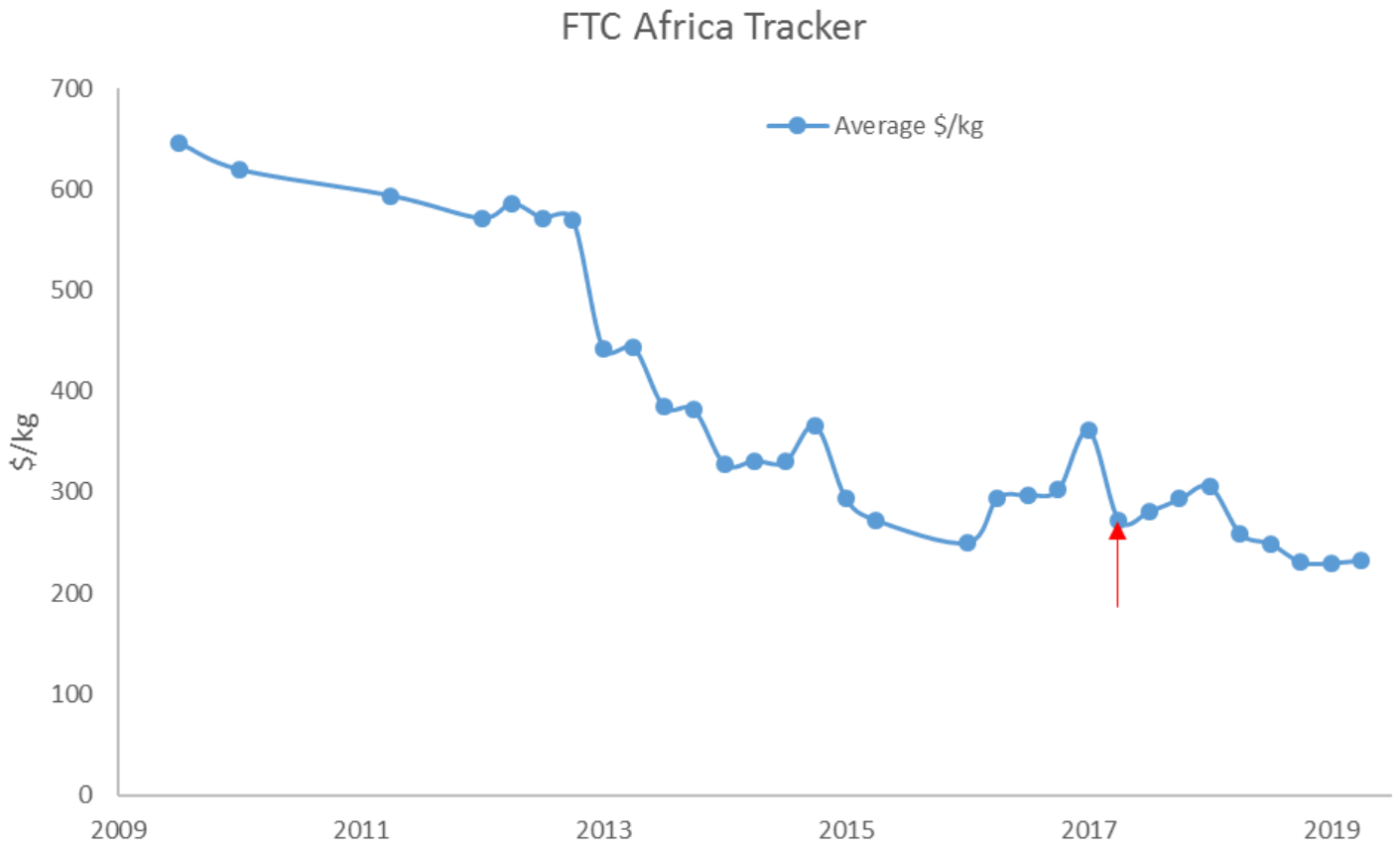
- Acyclic inexpensive starting materials
- Safer: No toxic starting materials
- Readily telescoped reactions
- High yielding reactions, 48% overall yield, further optimizations are underway
- Cost of raw materials to produce 5-FC is estimated to be reduced by 30-60%

M4ALL Route for 5-FC:



Emtricitabine (FTC) Price Tracking

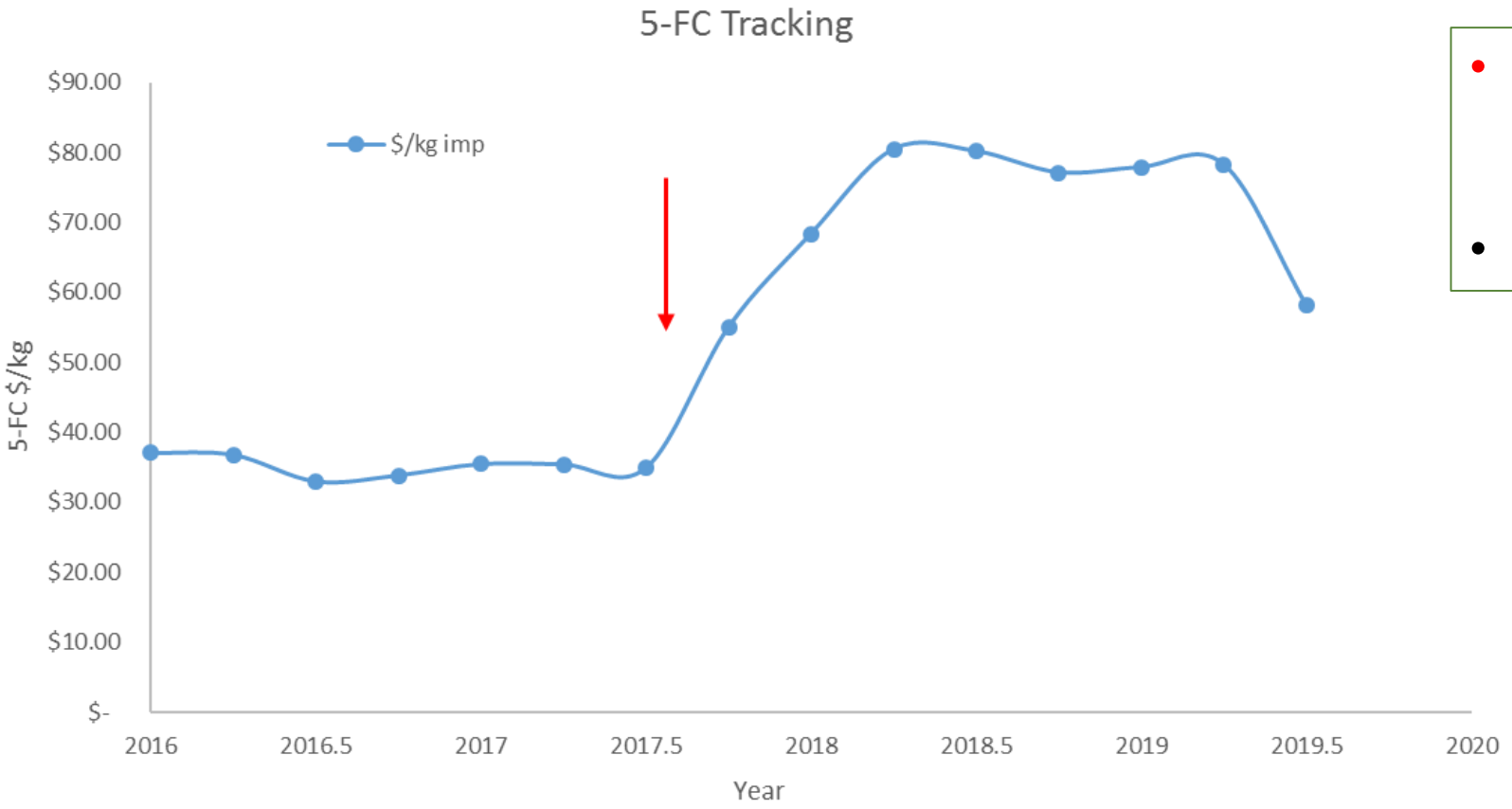
www.medicines4all.vcu.edu



- Chinese factory explosion affected supply and prices fluctuated.
- Prices don't appear to be as affected by the cytosine supply issues but this may be obscured by low demand volumes
- Current price ~ $232/kg

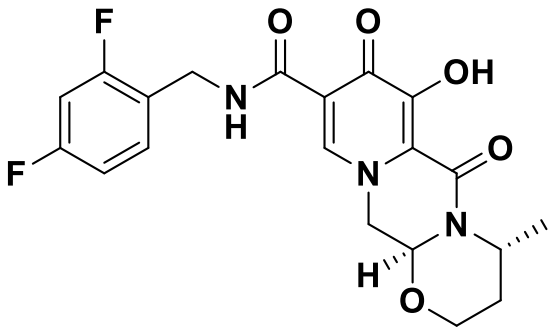
5-FC Price Tracking

www.medicines4all.vcu.edu



- Chinese factory explosion affected prices (arrow) and destabilized the market
- Current prices at ~ $58/kg

Dolutegravir (DTG) Example



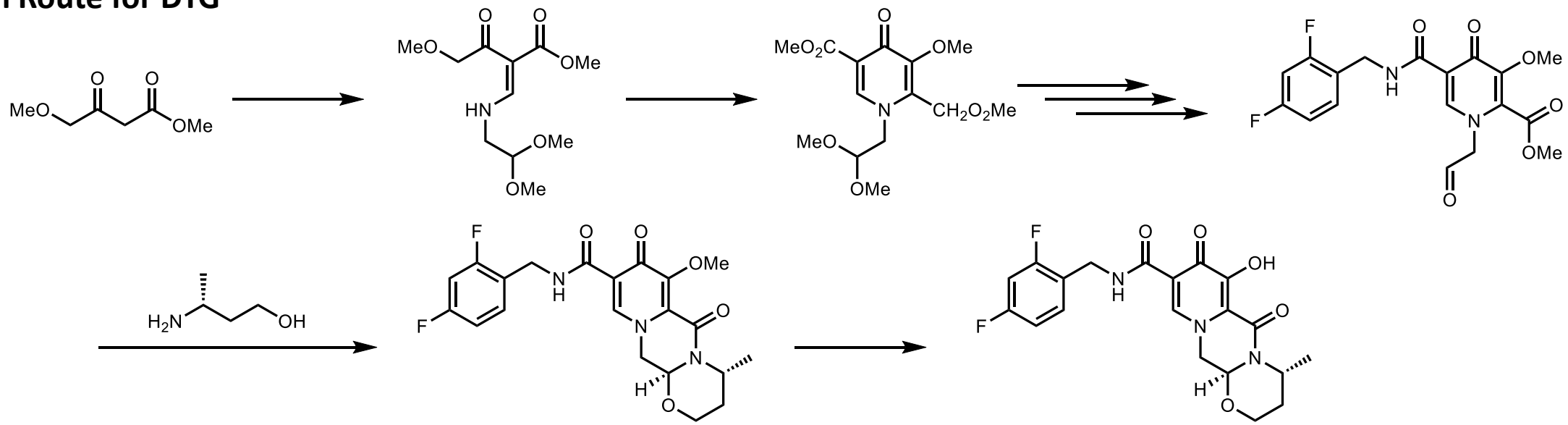
Dolutegravir (DTG)

Anti-HIV

HIV Integrase Inhibitor
Used as First-line Treatment

Volume sale: ~ 200 MT/year by 2020

Common Route for DTG



Dolutegravir Cost Drivers

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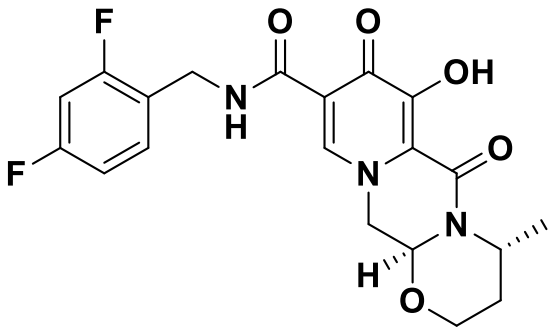


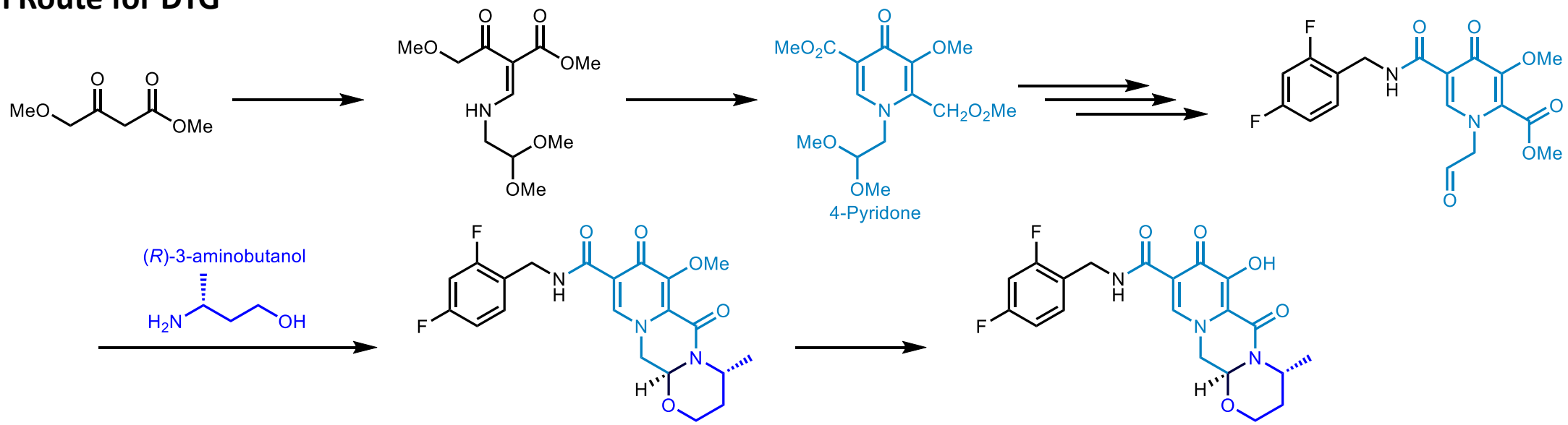
Dolutegravir (DTG)

Volume sale: ~ 200 MT/year by 2020

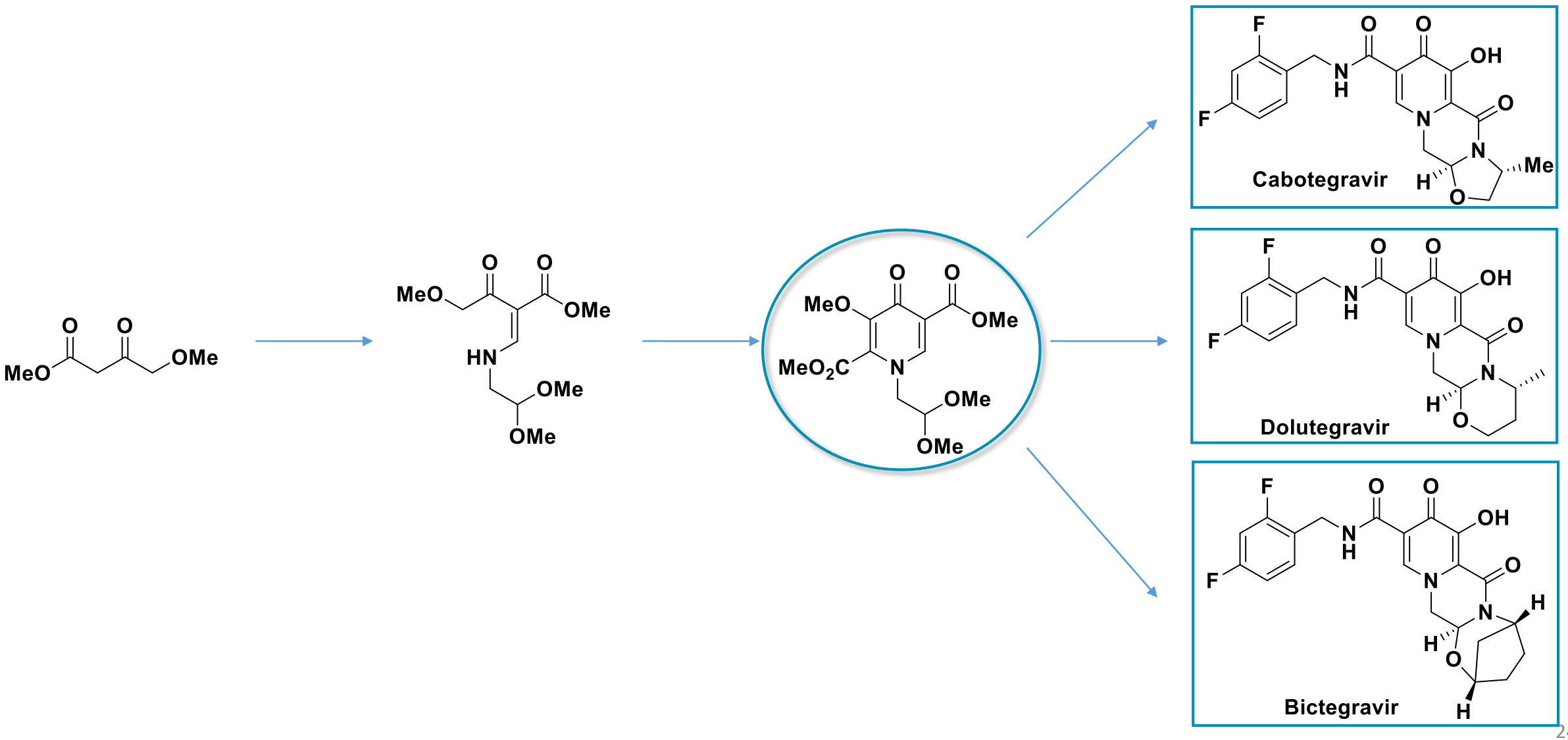
Anti-HIV

HIV Integrase Inhibitor
Used as First-line Treatment

Common Route for DTG



Dolutegravir Cost Drivers



WO 2015/019310 A1, WO 2016/125192 A2

Continuous Preparation of 4-Pyridone

medicines for all institute
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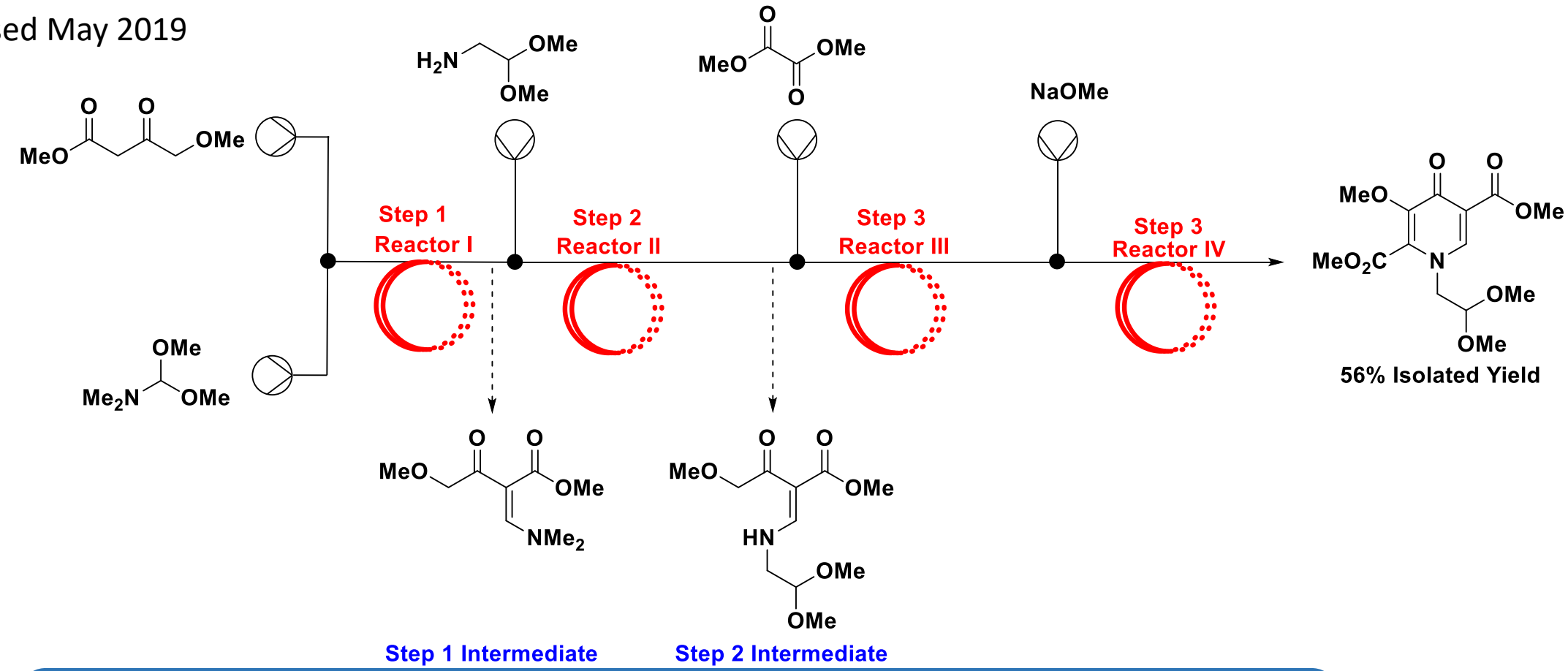
Released May 2019

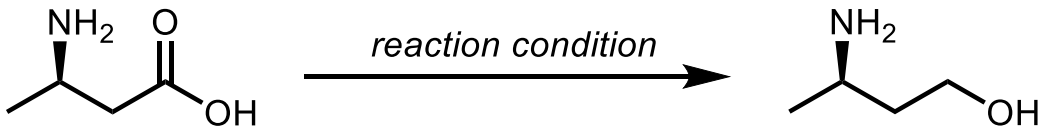


Telescoped Continuous Process offering significant cost reduction.
Improved Space-time Yield (69.3 g(L*h) (M4ALL) vs 1.19 g(L*h) (GSK).
Offers cost reduction of integrase inhibitors such as cabotegravir and bictegravir

M4ALL Preparation of (*R*)-3-aminobutanol

www.medicines4all.vcu.edu

Released November 2019



- **Isolated yield: 65-70%**
- **Use of inexpensive starting materials:**
  - **D-homo-β-alanine**
  - **Sodium aluminum hydride**

M4ALL Portfolio

www.medicines4all.vcu.edu

ARVs
- Nevirapine
- Tenofovir
- Dolutegravir
- Emtricitabine (FTC)
- Lamivudine (3TC)

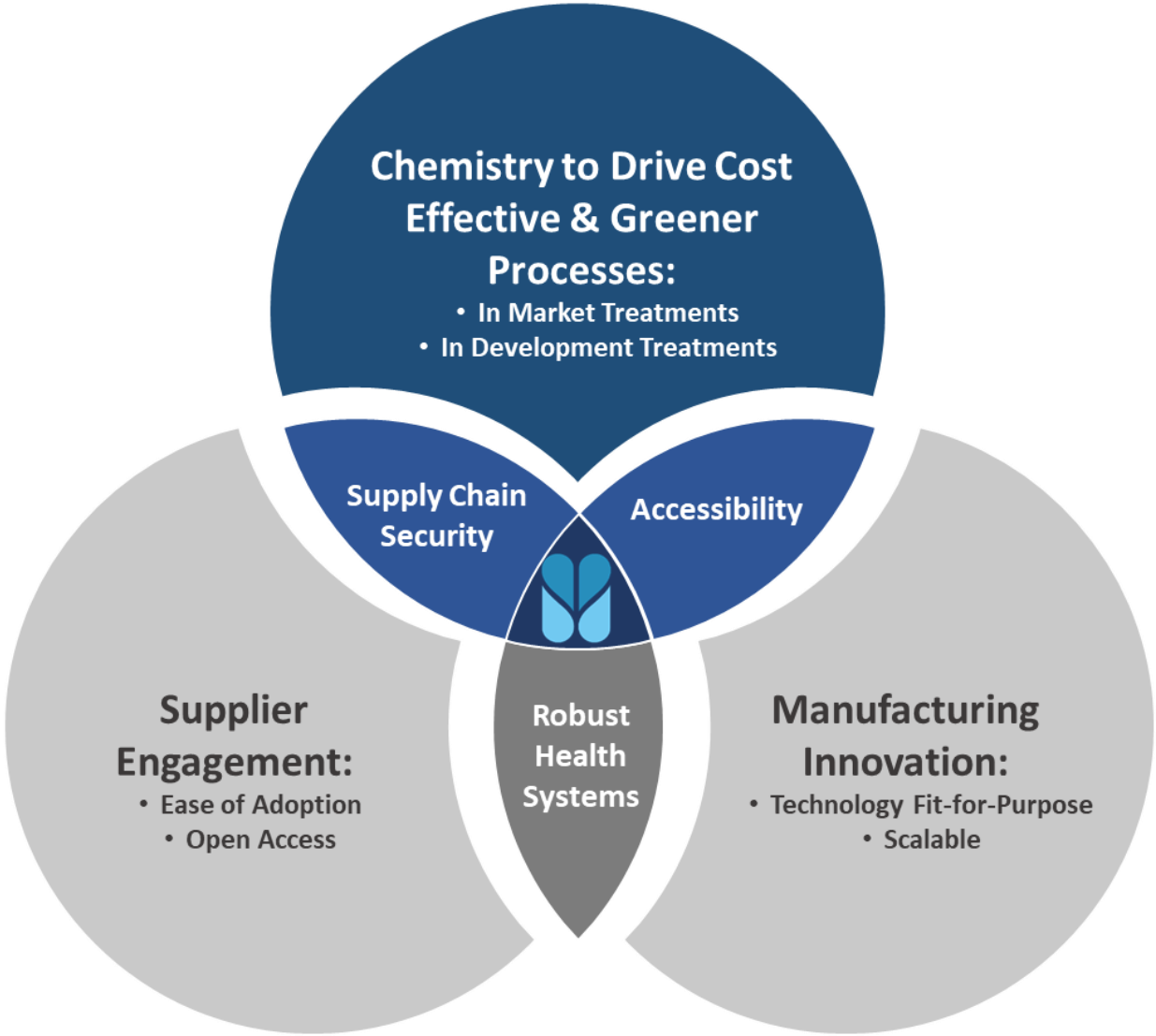
Tuberculosis
- In Development Treatments

Malaria
- In Development Treatments

Summary

www.medicines4all.vcu.edu

- We offer innovative solutions for procurers & suppliers to reduce the cost of medicines, strengthen the supply chain and enable accessibility to all
- Our demonstrated methodology works for both “in market” & “in development” treatments
- We engage in the entire lifecycle of processes, providing end-to-end ecosystem of offerings from cost analyses to optimized processes that reduce the cost of goods/manufacture



Thank You!

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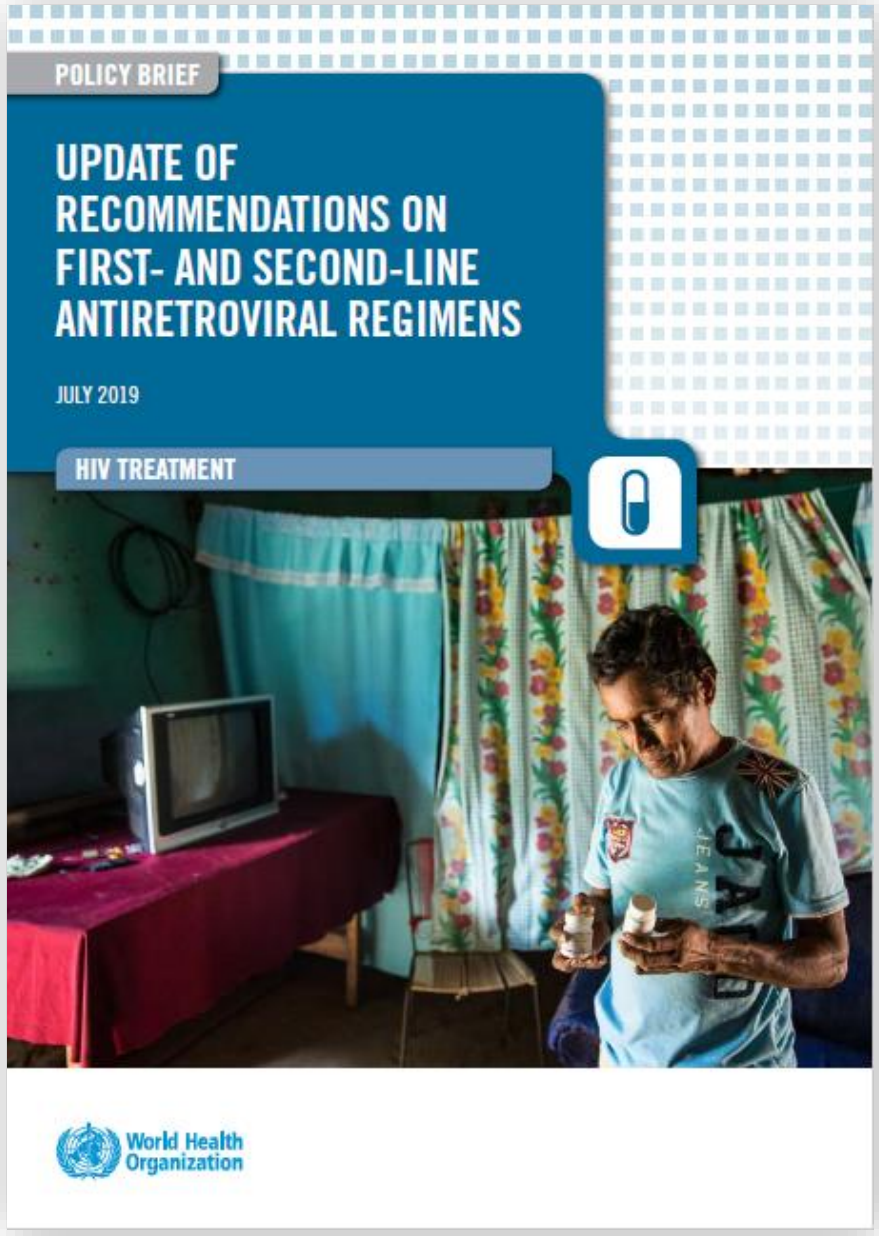


2019 WHO guidelines and future perspectives on ARV optimization

Marco Vitoria, WHO HQ

Annual ARV Buyer Seller Summit

24-27 Nov 2019

World Health Organization

WHO ARV Guidelines Evolution: 2002 to 2019

Topic	2002	2003	2006	2010	2013	2016	2018/2019
When to start	CD4 ≤200	CD4 ≤ 200	CD4 ≤ 200 - consider 350 - TB at CD4 ≤ 350	CD4 ≤ 350 - TB,HBV at any CD4	CD4 ≤ 500 - CD4 ≤ 350 as priority - TB, HBV, PW, SDC at any CD4	Treat All - CD4 ≤ 350 as priority - Programmatic focus on KPs	Treat All - Focus on KPs - **"Same day" start** - **Advanced HIV disease care package**
1st Line ART	8 options - AZT preferred	4 options - AZT preferred	8 options - AZT/TDF preferred - d4T dose reduction	6 options (FDC) - AZT/TDF preferred - d4T phase out	1 preferred option (FDC) - TDF/EFV preferred (all pops)	1 preferred option (FDC) - TDF/XTC/EFV preferred (all pops) - transition to new alternative ARV options (DTG, EFV_{400})	1 preferred option (FDC) - **TDF/3TC/DTG preferred (all pops)** - **TDF/3TC/EFV400 as alternative option** - **EFV600 and TAF in special situations**
2nd Line ART	Boosted and non-boosted PIs	Boosted PIs -IDV/r LPV/r, SQV/r	Boosted PIs - ATV/r, DRV/r, FPV/r LPV/r, SQV/r	Boosted PIs - Heat stable co-formulation: ATV/r, LPV/r	Boosted PIs -Heat stable co-formulation: ATV/r, LPV/r	Boosted PIs - Heat stable co-formulation: ATV/r, LPV/r - new alternative options (DRV/r, LPV/r + RAL)	**DTG as preferred 2nd line option** (if not used in 1st line) **ATV/r , DRV/r and LPV/r as alternative options** (preferred if DTG used in 1st line)
3rd Line ART	None	None	None	DRV/r, RAL, ETV	DRV/r, RAL, ETV	DRV/r, RAL, ETV, **DTG**	DRV/r, ETV, **DTG**
Viral Load Testing	No	No (Desirable)	Yes (Tertiary centers)	Yes (Phase in approach)	Yes (preferred for monitoring, use of PoC, DBS)	Yes (preferred for monitoring, scale up all technologies) **- CD4 monitoring can be stopped if patient virally supressed**	Yes (preferred for monitoring and **can be used for switching decision from TLE to TLD in stable patients**)

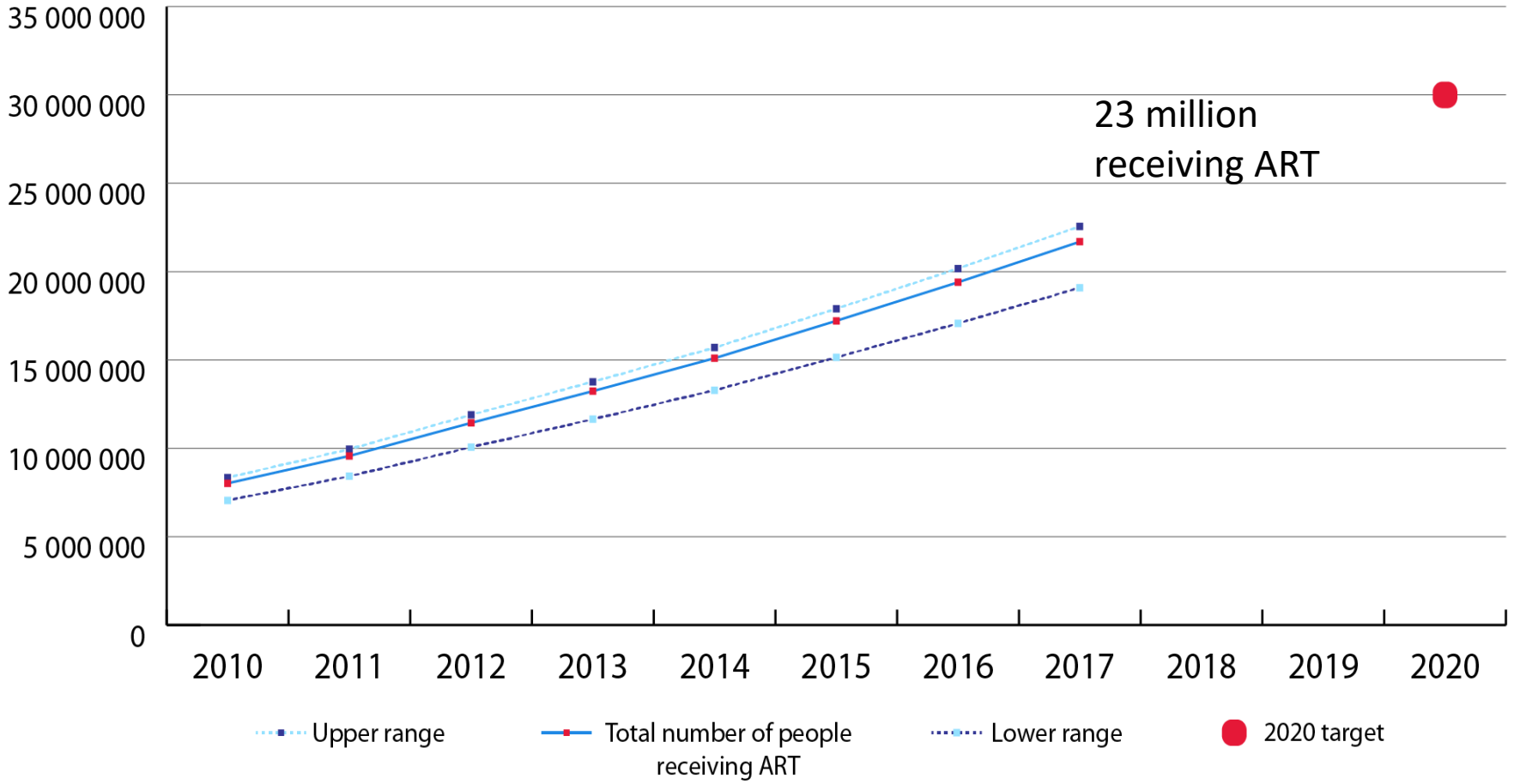
Earlier initiation

Simpler treatment

Less toxic, more robust regimens

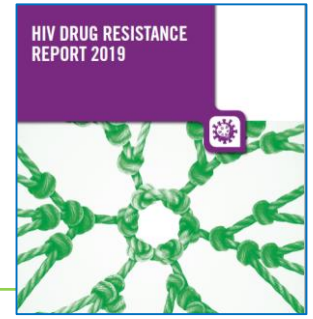
Better and simpler monitoring

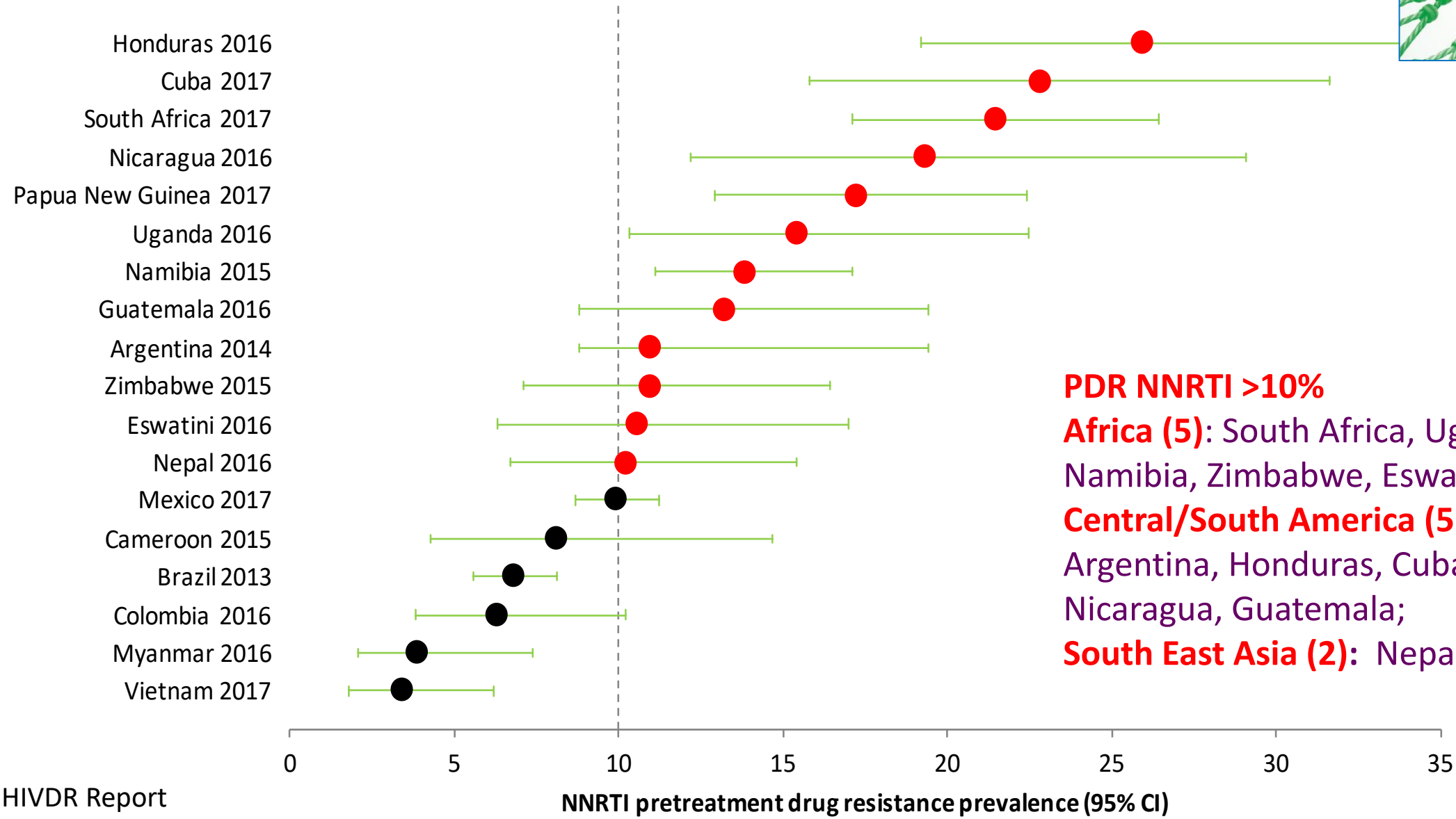
Increase in people receiving ART over time (62% ART coverage)



Source: UNAIDS/WHO estimates

Prevalence of PDR to NNRTI, by Country





PDR NNRTI >10%

Africa (5): South Africa, Uganda, Namibia, Zimbabwe, Eswatini;

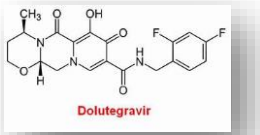
Central/South America (5): Argentina, Honduras, Cuba, Nicaragua, Guatemala;

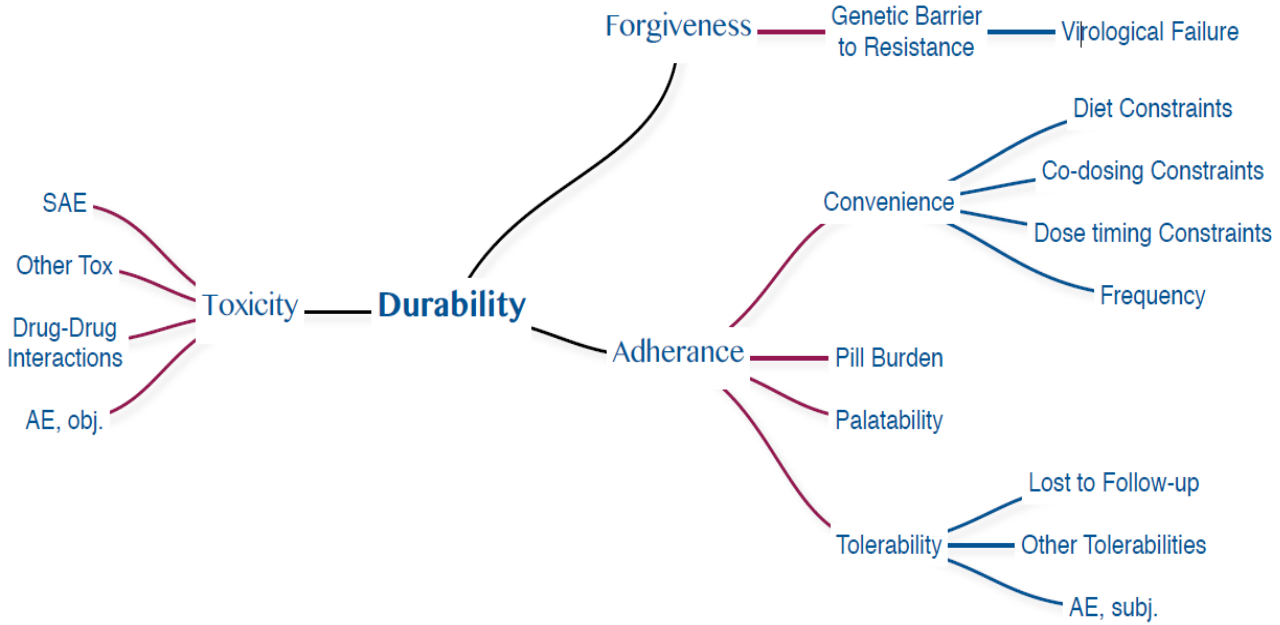
South East Asia (2): Nepal, PNG.

2019 WHO HIVDR Report

Dolutegravir – overall drug profile

- Integrase inhibitor (once daily dose)
- Effective (rapid viral load suppression)
- Well tolerated
- High genetic barrier to resistance
- Few drug interactions
- Single and fixed dose generic formulations
- Comparable price to current regimens used in LMICs (good potential for further reduction)





World Health Organization

Optimization profiles of new ARV drugs in WHO guidelines comparative analysis

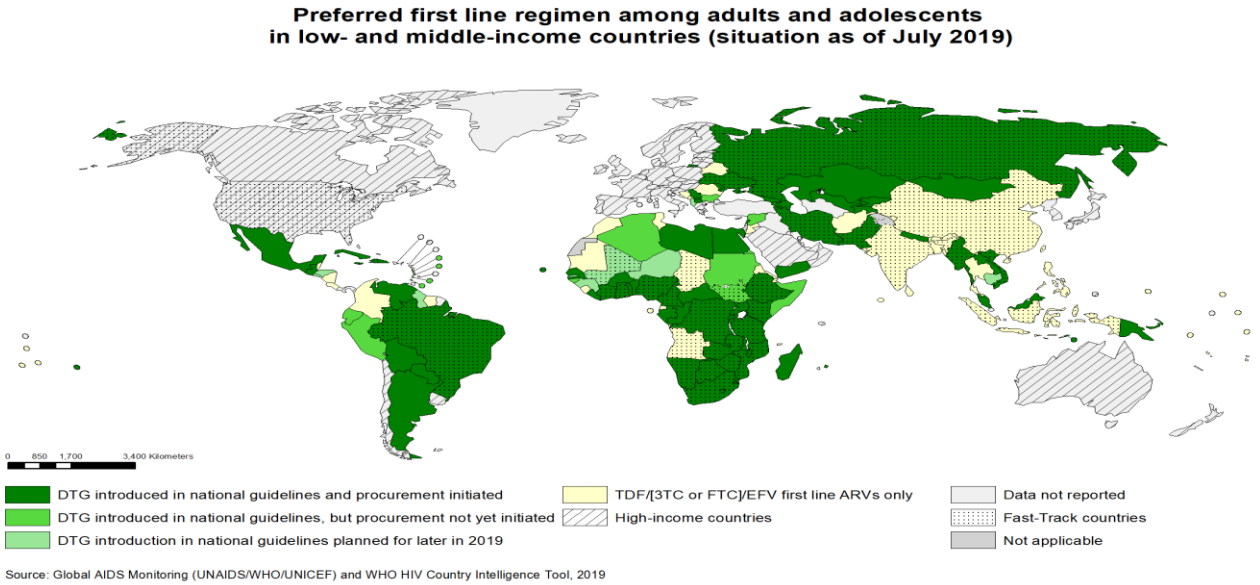
Optimization criteria		DTG	EFV_{400}	TAF	$DRV/r_{400/50}$
Efficacy and safety	Virologic potency				
	Lower toxicity				
	High genetic barrier to resistance				
Simplification	Available as generic FDC				
	Low pill burden/pill size				(*)
Harmonization	Use in pregnant women				
	Use in childbearing age women				
	Use in children				
	Use in HIV-associated TB				
	Few drug interactions				
Cost	Low price potential				

yes no ongoing studies

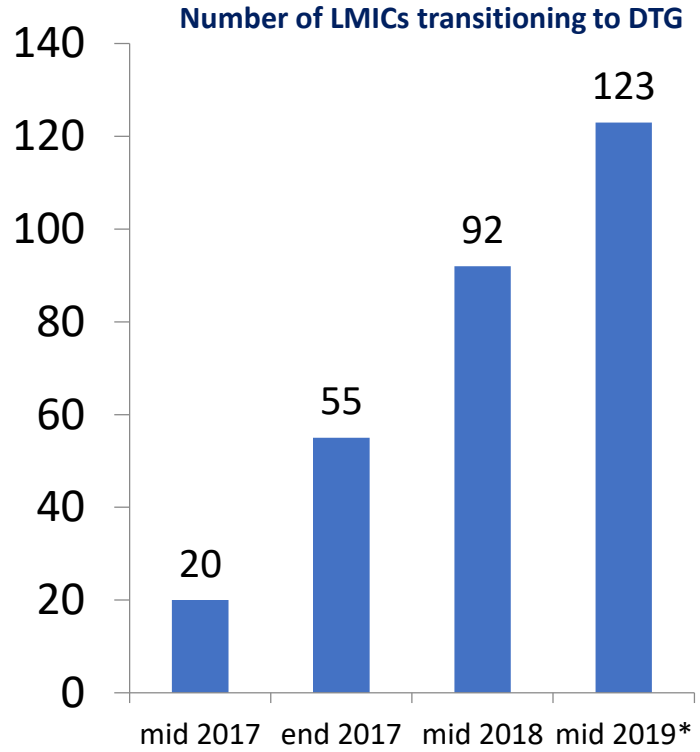
World Health Organization

* DRVr 400/100 OD has been studied.

DTG uptake by countries (mid-2019)



https://www.who.int/hiv/pub/arv/treat-all-uptake/en/



* WHO, preliminary data

- By mid 2019, **123 LMICs (90%) informed that have included or are planning to include DTG in their HIV treatment policy** :
  - TLD adopted as preferred 1st line option in national guidelines: 41
  - DTG introduced/introducing in national guidelines and procurement initiated: 82
- Approximately 4-5 million on PLHIV using DTG globally (accelerated uptake expected in 2019/2020)

New ARVs in WHO medicines lists (EML and EoI)

TLD and TLE400 in EML (page 20)
https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf?ua=1

TLD, TED, TEE400, TLE400, DRV/r in 17th HIV EoI (April2019)
https://extranet.who.int/prequal/sites/default/files/documents/EOI_HIV_April2019.pdf

World Health Organization

Topics in 2018/2019 that are influencing DTG transition

- NTD risk in WCBP using DTG (TSEPAMO study)
- Emerging adverse events potentially associated with DTG (and TAF): body weight gain and other metabolic effects (ADVANCE study)
- Transition in stable patients on TLE with and without VL (resistance risk)
- Sequencing to 2nd and 3rd line with DTG

2019 WHO ART Guidelines: What has been changed?

Topic	2018 interim guidelines	2019 updates
Use of DTG in 1st line	**DTG as preferred option** • Conditional recommendation • For **adults, adolescents and children with approved dosing** • Moderate certainty evidence for adults • **Very low certainty evidence for women of reproductive age** (note of caution on DTG and use of effective contraception)	**DTG as preferred option** • Strong recommendation • Moderate certainty evidence for **all** adults (programmatic considerations and informed by risk/benefit analysis for women of reproductive age) • Strong focus on women centred approach
Use of EFV in 1st line	**EFV 400 and EFV600 as alternative options** • Conditional recommendation • Moderate certainty of evidence • Limited evidence on EFV400 efficacy in TB and pregnant women	**EFV400 as alternative option (including TB and PW)** • Strong recommendation • Moderate certainty of evidence **EFV600 used in special situations**
Use of DTG in 2nd line	**DTG as preferred option if not used in 1st line** • Conditional recommendation • Moderate certainty of evidence (note of caution on DTG use for women of reproductive age)	**DTG as preferred option if not used in 1st line** • Conditional recommendation • Moderate certainty of evidence (informed by risk/benefit analysis for women of reproductive age) **PI as preferred option if DTG used in 1st line** • Strong recommendation • Moderate certainty of evidence

World Health Organization

PICO questions for 2019 update

DTG in 1st line

- **PICO 1a**: Should **DTG-based** regimens be recommended as the **preferred first-line** with an NRTI backbone for the treatment of HIV in adults and adolescents?

NEW

- **PICO 1b**: Should **PI-based regimens** be recommended as the alternative first-line for the treatment of HIV in **women and adolescent girls** of childbearing potential in settings with poor access to contraception and **high levels of NNRTI resistance**?

DTG in 2nd line

- **PICO 2:**Should **DTG** be recommended as the **preferred second-line** antiretroviral agent in combination with an optimized NRTI backbone for the treatment of HIV?

Role of EFV_{400}

- **PICO 3**: Should **EFV_{400}** be used as an **alternative to EFV_{600}** in combination with an NRTI backbone for the treatment of HIV in adults and adolescents?

NEW

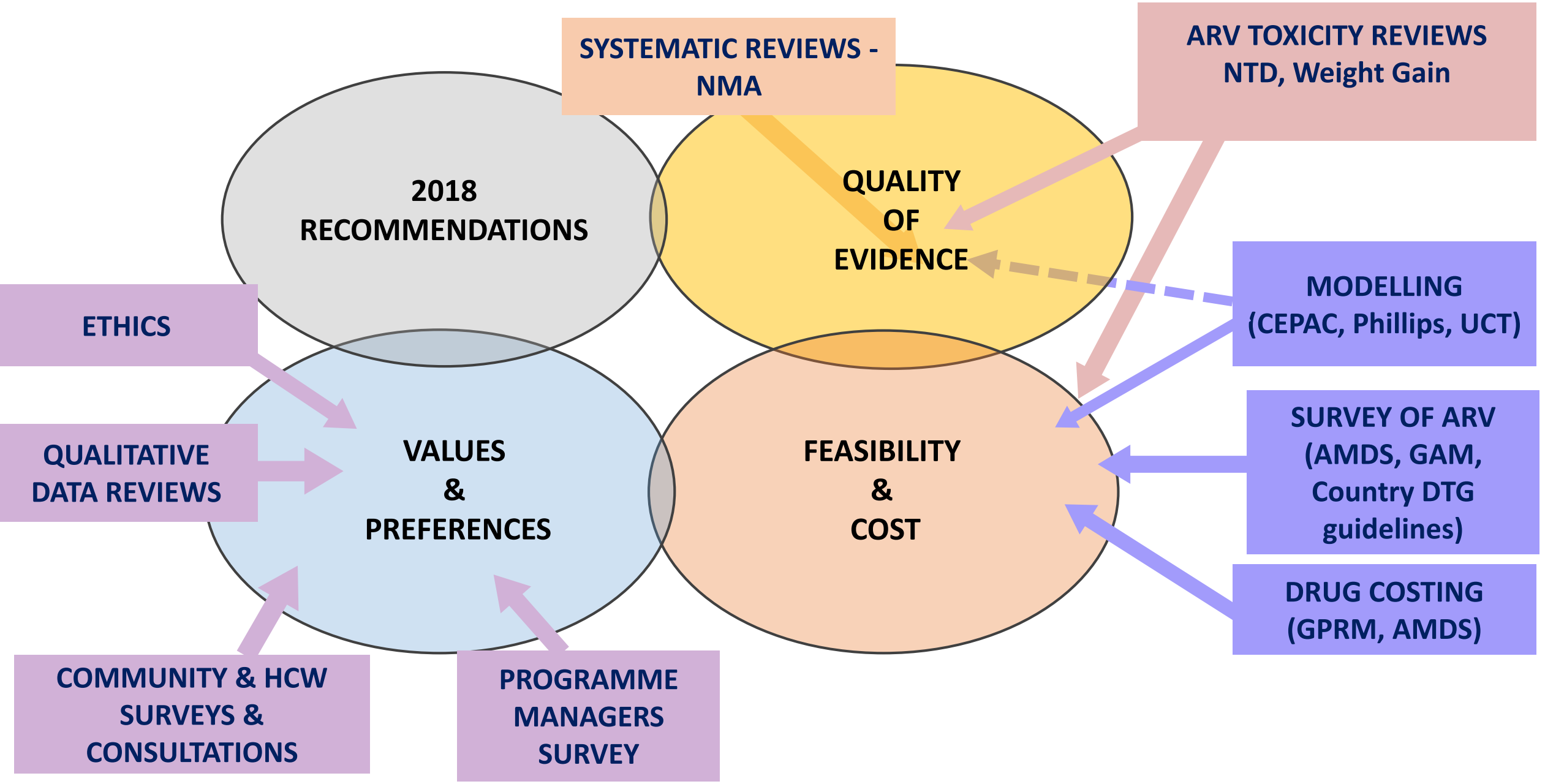
Role of TAF

- **PICO 4:** Should **TAF** be used as an **alternative to TDF** in combination with 3TC (or FTC) in the NRTI backbone for the treatment of HIV?

What is new relative to 2018 review?

- New data from key studies (ADVANCE, DAWNING, DOLPHIN, NAMSAL, TSEPAMO) – some data is confidential
- Additional outcomes were included/expanded
  - Time to VL suppression
  - Maternal & birth outcomes (including NTDs)
  - Adverse events: body weight gain, CNS, bone, renal and metabolic effects (grade 3-4)
- More subpopulations: women and adolescents in childbearing age

2019 ARV Guidelines Process



Safety and Efficacy of DTG and EFV_{600} in 1st line ART
(summary 2019 WHO Sys Review & NMA)

	major outcomes	DTG vs EFV_{600}	quality of evidence
Efficacy outcomes	Treatment discontinuation (any or due AEs)	DTG better	high
	Viral suppression (4-96 weeks), viral suppression at delivery (PW), transmission (PW)	DTG probably better	high to moderate
	CD4 recovery (24-144 weeks)	DTG probably better	high to moderate
	Mortality	comparable	low
Tolerability, safety & resistance outcomes	Neuropsychiatric AEs (any grade), depression (grade 3 or 4), dizziness (any grade)	DTG probably better	moderate to low
	Sleep disorders (any grade)	comparable	very low
	Body weight gain	EFV probably better	moderate
	NTD	EFV may be better	low
	HIVDR (overall, NRTI or anchor drug)	DTG probably better	high to moderate

Reference: Steve Kanters, For WHO ARV GDG, 5-7 June 2019

World Health Organization

Safety and Efficacy of EFV_{400} and EFV_{600} in 1st line ART (PICO 3)

(summary 2019 WHO Sys Review & NMA)

	major outcomes	EFV_{400} vs EFV_{600}	quality of evidence
Efficacy outcomes	Treatment discontinuation (due AEs)	EFV400 better	high to moderate
Efficacy outcomes	Viral suppression (48-96 weeks), VL suppression if baseline > 100,000 (48 weeks)	comparable	moderate
Efficacy outcomes	CD4 recovery (24-96 weeks)	comparable	moderate
Efficacy outcomes	Mortality	comparable	low
Tolerability, safety & resistance outcomes	Neuropsychiatric AEs (any grade), depression (grade 3 or 4), dizziness (any grade), sleep disorders (any grade)	comparable	low to very low
Tolerability, safety & resistance outcomes	Body weight gain	comparable	low
Tolerability, safety & resistance outcomes	Treatment related adverse events	EFV400 better	moderate
Tolerability, safety & resistance outcomes	HIVDR (overall, NRTI or anchor drug)	comparable	very low

Reference: Steve Kanters, For WHO ARV GDG, 5-7 June 2019

World Health Organization

2019 WHO recommendations: First-line ART regimens

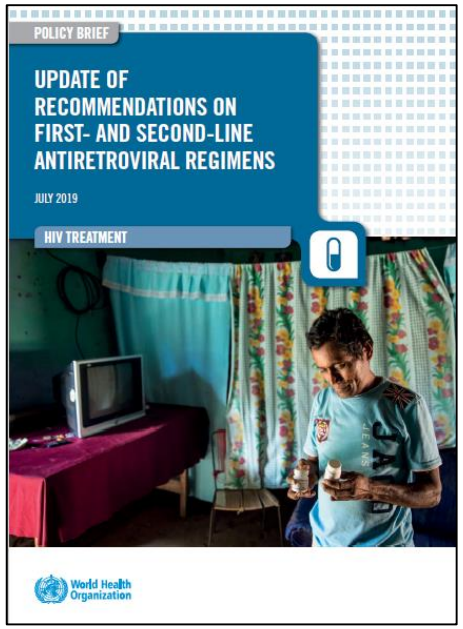


Table 1. Preferred and alternative first-line ART regimens

Population	Preferred first-line regimen	Alternative first-line regimen	Special circumstances
Adults and adolescents	TDF + 3TC (or FTC) + DTG[a]	TDF + 3TC + EFV 400 mg[b]	TDF + 3TC (or FTC) + EFV 600 mg[b] AZT + 3TC + EFV 600 mg[b] TDF + 3TC (or FTC) + PI/r[b] TDF + 3TC (or FTC) + RAL TAF[c] + 3TC (or FTC) + DTG ABC + 3TC + DTG[a]
Children	ABC + 3TC + DTG[d]	ABC + 3TC + LPV/r ABC + 3TC + RAL[e] TAF + 3TC (or FTC) + DTG[f]	ABC + 3TC + EFV (or NVP) AZT + 3TC + EFV[g] (or NVP) AZT + 3TC + LPV/r (or RAL)
Neonates	AZT + 3TC + RAL[h]	AZT + 3TC + NVP	AZT + 3TC + LPV/r[i]

3TC: lamivudine; ABC: abacavir; AZT: zidovudine; DTG: dolutegravir; EFV: efavirenz; FTC: emtricitabine; LPV/r: lopinavir/ritonavir; NVP: nevirapine; PI/r: protease inhibitor boosted with ritonavir; RAL: raltegravir; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate.

[a]Effective contraception should be offered to adult women and adolescent girls of childbearing age or potential. DTG can be prescribed for adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in the risk of neural tube defects (at conception and until the end of the first trimester). If women identify pregnancy after the first trimester, DTG should be initiated or continued for the duration of the pregnancy (Box 2).

[b]EFV-based ART should not be used in settings with national estimates of pretreatment resistance to EFV of 10% or higher. DTG-based ART is preferred, and if DTG is unavailable, a boosted PI-based regimen should be used. The choice of PI/r depends on programmatic characteristics.

[c]TAF may be considered for people with established osteoporosis and/or impaired kidney function.

[d]For age and weight groups with approved DTG dosing.

[e]RAL should be used as an alternative regimen only if LPV/r solid formulations are not available.

[f]For age and weight groups with approved TAF dosing.

[g]EFV should not be used for children younger than three years of age.

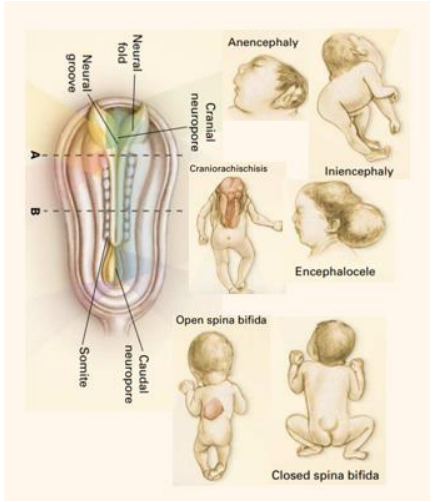
[h]Neonates starting ART with an RAL-based regimen should transition to an LPV/r solid formulation as soon as possible.

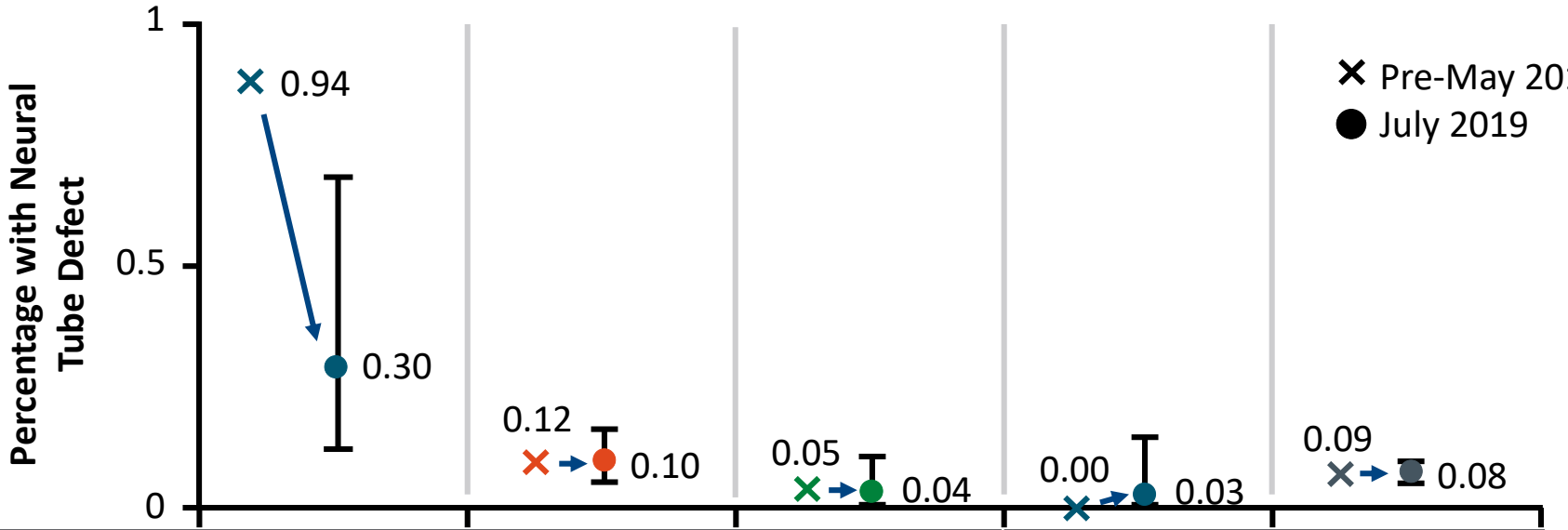
[i]LPV/r syrup or granules can be used if starting after two weeks of age.

World Health Organization

Tsepamo: Prevalence of NTDs by ARV Exposure

Different phenotypes of neural tube defects





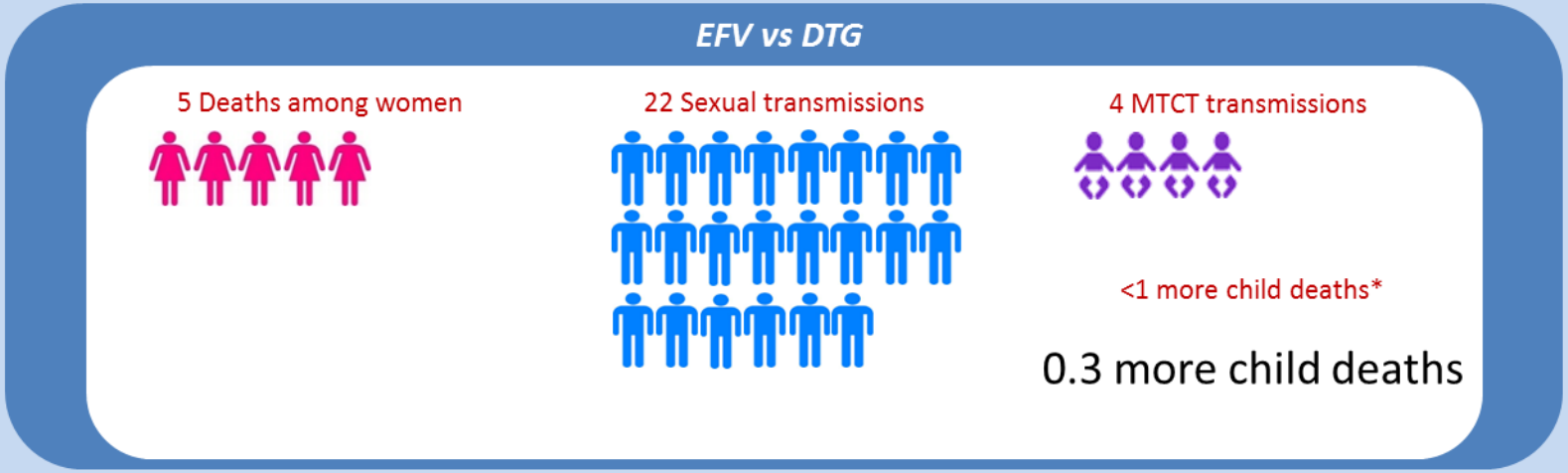
	Conception			Pregnancy	HIV Negative (n = 89,372)
	DTG (n = 1683)	Non-DTG (n = 14,792)	EFV (n = 7959)	DTG (n = 3840)	
Total NTDs per exposures, n/N	5/1683	15/14792	3/7959	1/3840	70/89372
▪ Prevalence difference, % (95% CI)	Ref	0.20 (0.01-0.59)	0.26 (0.07-0.66)	0.27 (0.06-0.67)	0.22 (0.05-0.62)
NTDs per exposures since May 2018, n/N	1/1275	1/3492	0/2172	1/1028	9/23,315

Zash. IAS 2019. Abstr MOAX0105LB.

Slide credit: clinicaloptions.com

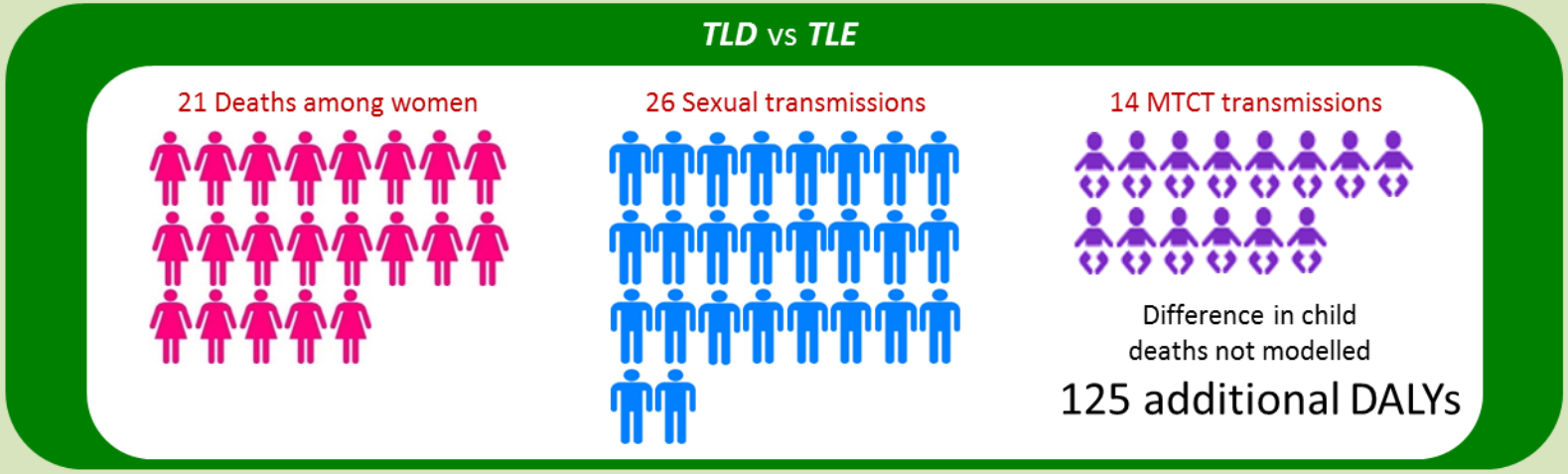
CEPAC: Tsepamo May 2019 NTD risk, NMA ARV efficacy, PDR 10.7%

For every 1 NTD averted with use of *EFV* compared to *DTG*, it is predicted that there will be this many additional outcomes:



SYNTHESIS: Tsepamo May 2019 NTD risk, incl. ADVANCE/NAMSAL, PDR 9%

For every 1 adverse infant outcome (NTD+NND) averted with use of *TLE* compared to *TLD*, it is predicted that there will be this many additional outcomes:



Both models show that use of EFV for WCP initiating ART rather than DTG in order to avoid NTDs (& NNDs) would likely lead to other substantial negative impacts at population level.


ORIGINAL RESEARCH Annals of Internal Medicine

Risks and Benefits of Dolutegravir- and Efavirenz-Based Strategies for South African Women With HIV of Child-Bearing Potential

A Modeling Study

Caitlin M. Dugdale, MD; Andrea L. Ciaranello, MD, MPH; Linda-Gail Bekker, MD, PhD; Madeline E. Stern, BA; Landon Myer, MBChB, PhD; Robin Wood, MMed, DSc (Med); Paul E. Sax, MD; Elaine J. Abrams, MD; Kenneth A. Freedberg, MD, MSc; and Rochelle P. Walensky, MD, MPH

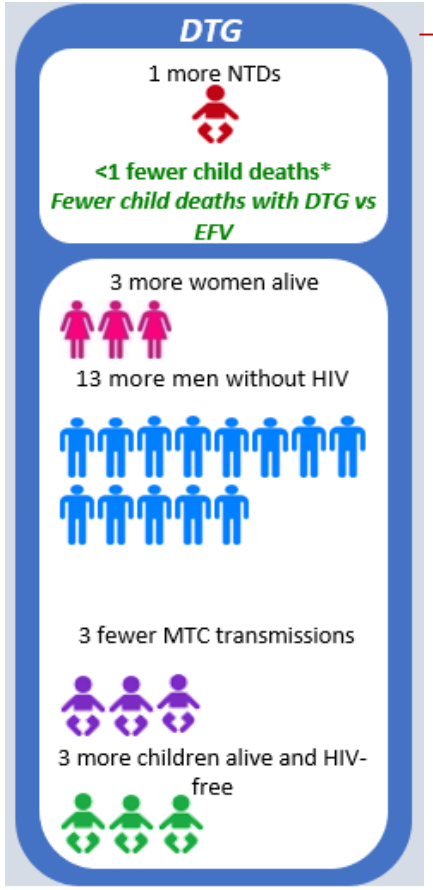
Risk vs Benefits of DTG in Women of Childbearing-Potential at a Population Level

Dugdale C et al. Ann Int Med. 2019 – Updated for June 2019 GDG meeting with updated data

CEPAC: May 2019 Tsepamo data 0.3% NTD; NNRTI pretreatment drug resistance 10.7%; DTG efficacy per recent trials

For every 1000 South African women of childbearing potential with HIV **starting ART**, per yr, compared with ***EFV (average over 5 yrs)***:

DTG only vs EFV only



*n<0.5;

→ "DTG in all" compared to "EFV in all" in 1,000 women of childbearing potential:

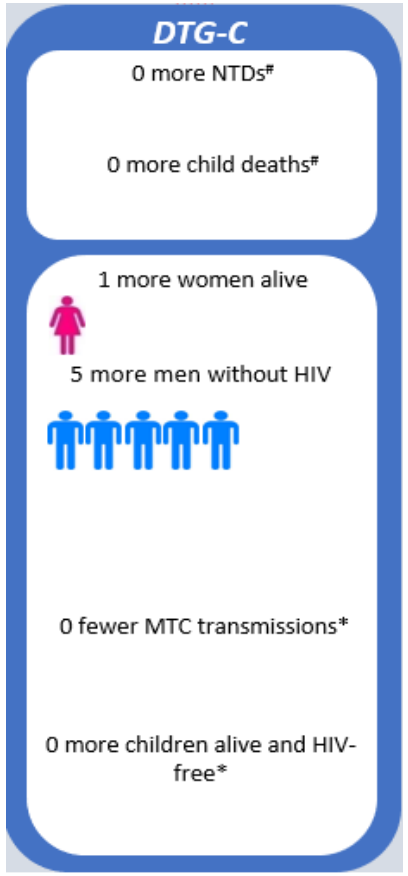
- 1 excess NTD
- More maternal survival, less transmission to sexual partners, less MTCT, resulting in higher HIV-free survival in infants

→ "DTG with contraceptive" vs EFV in 1,000 women of childbearing potential

- Reducing unintended pregnancies in women using DTG effectively eliminates NTD concerns
- Still more maternal survival and less transmission to sex partners
- Needs high coverage of effective contraceptive methods
- Reducing unintended pregnancies important goal of integrating contraceptive & family planning services into ART

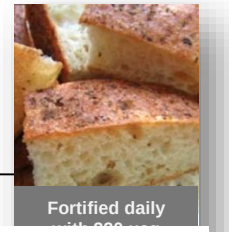
Source: C Dugdale/WHO 2019

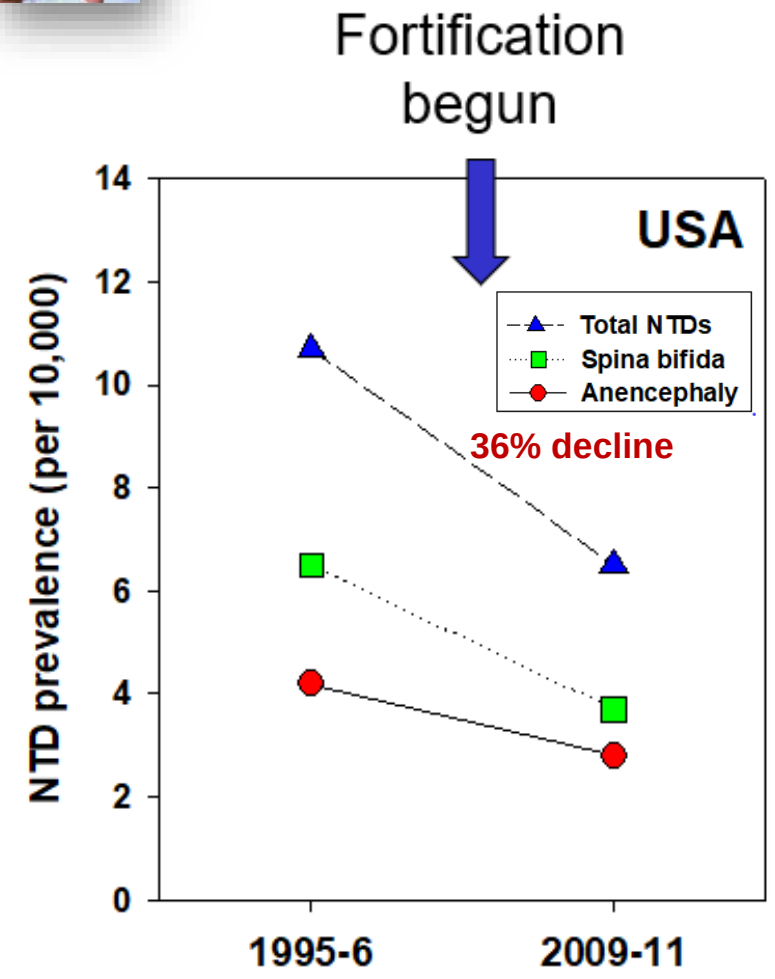
DTG with contraception vs EFV only



#n=0; numbers ≥0.5 rounded up

Folate Food Fortification and NTD risk





Williams, MMWR, 2015

Table 2. Regional meta-analysis of overall birth prevalence of neural tube defects

Region	Number of studies	Overall NTD birth prevalence per 10,000 live births	95% Confidence intervals
Australasia	1	12.10	10.45–13.94
Latin America and the Caribbean: with folic acid fortification	12	7.78	6.58–8.97
Latin America and the Caribbean: without folic acid fortification	1	22.89	18.01–28.69
Eastern Europe and Central Asia	6	9.92	7.6–12.24
Sub-Saharan Africa: with folic acid fortification[a]	1	9.95	7.26–13.30
Sub-Saharan Africa: without folic acid fortification	6	15.27	10.19–20.34
East Asia	9	19.44	15.46–23.41
Northern Africa and Western Asia[b]	9	17.45	13.56–21.34
Europe	17	8.63	6.80–10.47
Southeast Asia[c]	2	6.76	5.77–7.75
North America	NA	Both countries in region have data	
Southern Asia[d]	11	31.96	23.81–40.12

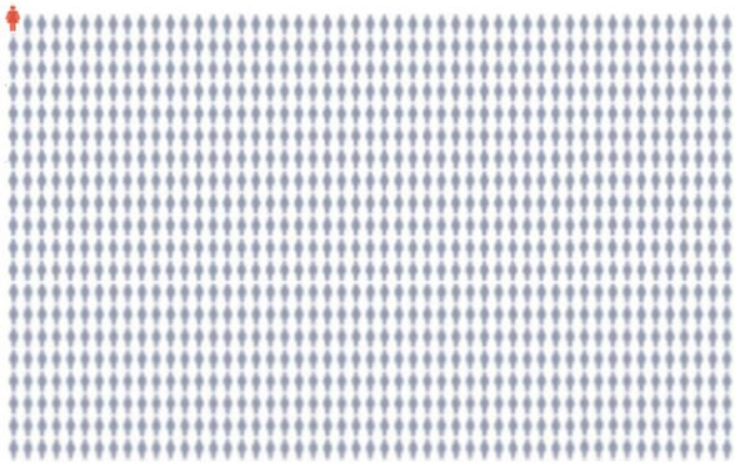
66% decline

[a]Based on a single South African study.[1]
[b]Studies are highly heterogeneous. Pooled regional data regardless of folic fortification (see Appendix S6, online only).
[c]Likely underestimate: used pooled hospital-based data from SEARO Newborn and Birth Defects Database in estimates.[2]
[d]Iran is the only country in the region with high coverage of folic fortification; we assumed that South Africa postfortification rates apply.[1]

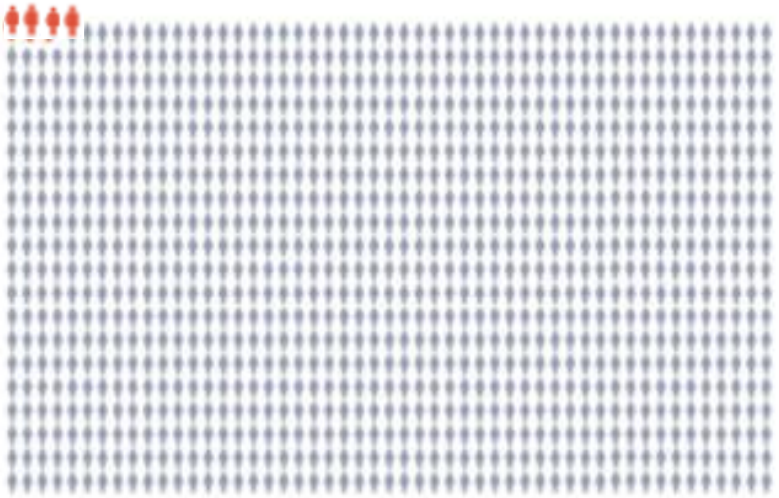
Blencowe H et al. Ann NY Acad Sci 2018

- **It is important to recognize**
  - Neural tube defect risk is not zero in the absence of drug
  - The risk, if confirmed, is still relatively small
  - For example, with APR prevalence of 0.4%: 1 in 1000 in the general population without folate food fortification with potential increase to 4 in 1000 – an excess of 3 NTD per 1,000 exposures

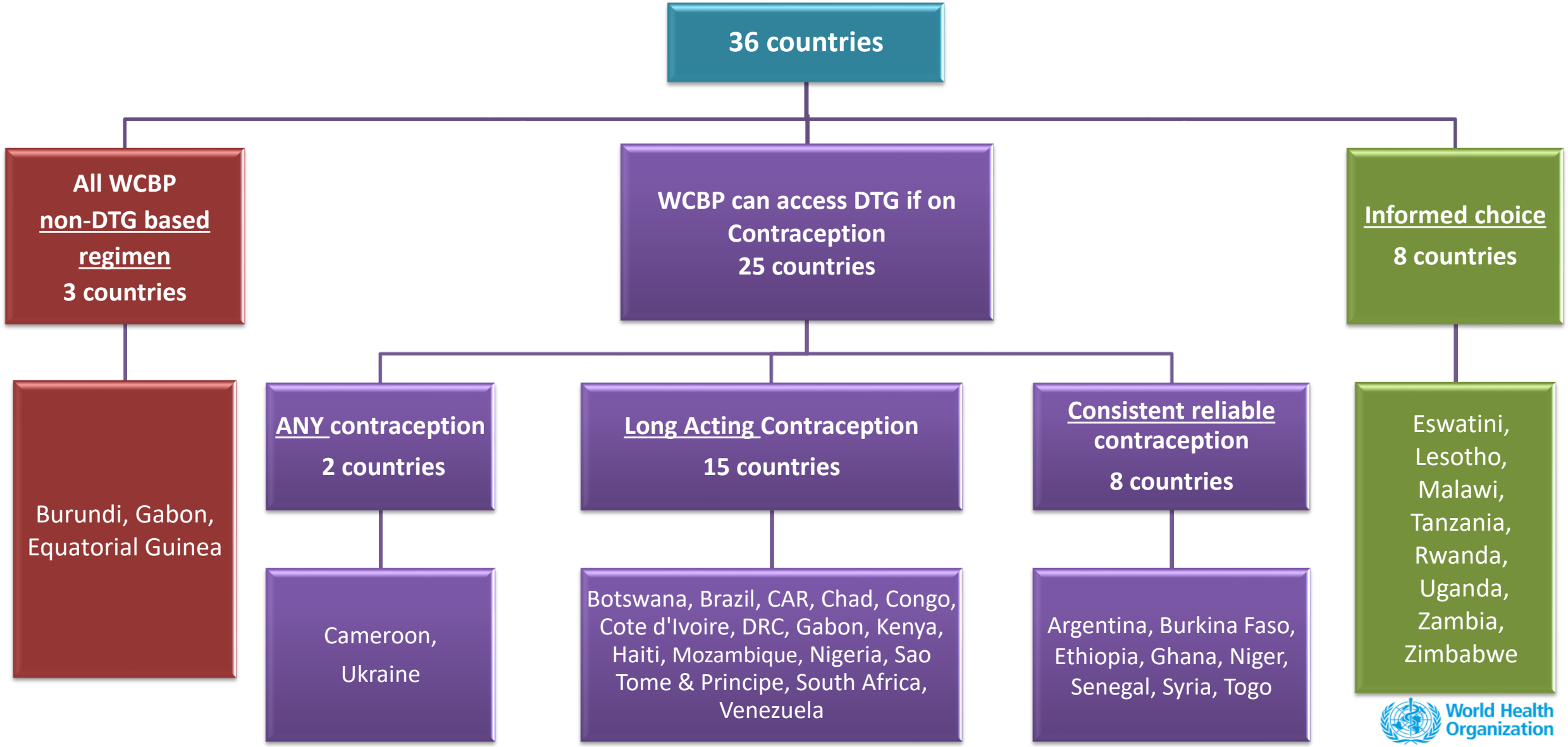
No drug exposure
No food folate fortification:
NTD prevalence 0.1%



NTD with DTG prevalence in APR
0.40% =
increase of 3 NTD per 1000 exposures



Access to DTG as preferred 1st line among WCBP in 36 LMICs, Nov 2019 (preliminary data - Nov 2019)



World Health Organization

Safety and Efficacy of DTG and PIs (LPVr) in 2nd line ART

(summary 2019 WHO Sys Review & NMA)

	major outcomes	DTG vs LPVr	quality of evidence
Efficacy outcomes	Viral suppression (4-96 weeks)	DTG better	high
	Viral suppression baseline VL > 100,000 (48 weeks)	comparable	moderate
	CD4 recovery (24-48 weeks)	comparable	moderate
	Mortality	comparable	low
Tolerability, safety & resistance outcomes	Neuropsychiatric AEs (any grade)	comparable	low
	Treatment related SAE	comparable	low
	Treatment emergent AE, related AEs	DTG probably better	high
	Treatment discontinuation (any or due AEs)	DTG probably better	high
	HIVDR (overall)	comparable	very low

Reference: Steve Kanters, For WHO ARV GDG, 5-7 June 2019

World Health Organization

2019 WHO recommendations: Second-line ART regimens

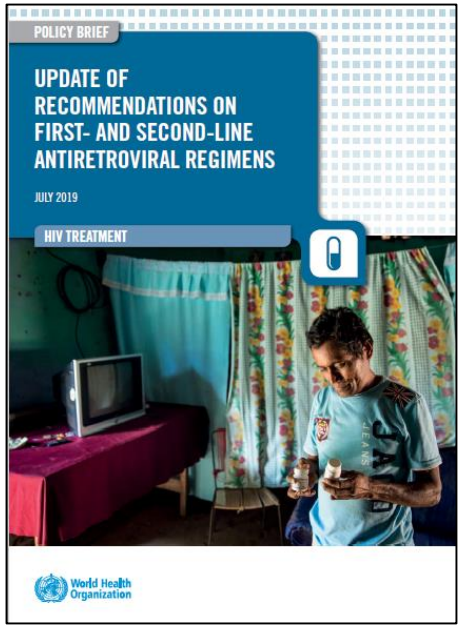


Table 2. Preferred and alternative second-line ART regimens

Population	Failing first-line regimen	Preferred second-line regimen	Alternative second-line regimens
Adults and adolescents[a]	TDF[b] + 3TC (or FTC) + DTG[c]	AZT + 3TC + ATV/r (or LPV/r)	AZT + 3TC + DRV/r[d]
	TDF + 3TC (or FTC) + EFV (or NVP)	AZT + 3TC + DTG[c]	AZT + 3TC + ATV/r (or LPV/r or DRV/r)[d]
	AZT + 3TC + EFV (or NVP)	TDF[b] + 3TC (or FTC) + DTG[c]	TDF[b] + 3TC (or FTC) + ATV/r (or LPV/r or DRV/r)[d]
Children and infants	ABC + 3TC + DTG[e]	AZT+ 3TC + LPV/r (or ATV/r[f])	AZT + 3TC + DRV/r[g]
	ABC (or AZT) + 3TC + LPV/r	AZT (or ABC) + 3TC + DTG[e]	AZT (or ABC) + 3TC + RAL
	ABC (or AZT) + 3TC + EFV	AZT (or ABC) + 3TC + DTG[e]	AZT (or ABC) + 3TC + LPV/r (or ATV/r[f])
	AZT + 3TC + NVP	ABC + 3TC + DTG[e]	ABC + 3TC + LPV/r (or ATV/r[f] or DRV/r[g])

3TC: lamivudine; ABC: abacavir; ATV/r: atazanavir/ritonavir; AZT: zidovudine; DRV/r: darunavir/ritonavir; DTG: dolutegravir; EFV: efavirenz; FTC: emtricitabine; LPV/r: lopinavir/ritonavir; NVP: nevirapine; RAL: raltegravir; TDF: tenofovir disoproxil fumarate.

[a]Sequencing if PIs are used in first-line ART: ATV/r (or LPV/r or DRV/r depending on programmatic considerations) + TDF + 3TC (or FTC) and then AZT + 3TC + DTG in second-line ART.

[b]Effective contraception should be offered to adult women and adolescent girls of childbearing age or potential. DTG can be prescribed for adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in the risk of neural tube defects (at conception and until the end of the first trimester). If women identify pregnancy after the first trimester, DTG should be initiated or continued for the duration of the pregnancy (Box 2).

[c]TAF (tenofovir alafenamide) can be used as an alternative NRTI in special situations for adults and adolescents.

[d]RAL + LPV/r can be used as an alternative second-line ART regimen for adults and adolescents.

[e]The European Medicines Agency currently only approves DTG for children weighing at least 15 kg and more widely for children weighing more than 20 kg who can take adult 50-mg film-coated tablets. Studies are ongoing to determine dosing for younger children, with approval expected in early 2020, but the 2016 WHO recommendations for second-line ART still hold (PI-based for children for whom NNRTIs have failed and RAL for children for whom LPV/r has failed). TAF (tenofovir alafenamide) can be used as an alternative NRTI in children weighing at least 25 kg.

[f]ATV/r can be used as an alternative to LPV/r for children older than three months, but the limited availability of suitable formulations for children younger than six years, the lack of a fixed-dose formulation and the need for separate administration of the ritonavir booster should be considered when choosing this regimen.

[g]DRV should not be used for children younger than three years and should be combined with appropriate dosing of ritonavir.

World Health Organization

TLD transition at a glance

Treatment transition scenario		Preferred approach
DTG in people living with HIV initiating ART		
Adult men, post-menopausal women and adolescent boys		Initiate TLD
Pregnant/Breastfeeding women and adolescent girls		Initiate TLD
Women and adolescent girls of childbearing age potential		Initiate TLD + informed decision on use of contraception and folate supplementation
Children	if body weight ≥ 20 kg	Initiate ABC/3TC + DTG (20-29.9 kg) or TLD (≥ 30 kg)
	if body weight < 20 kg	Initiate ABC/3TC + LPV/r
TB co-infection		Initiate TLD (DTG BD)
DTG in people living with HIV already using first-line regimen		
Clinical/immunological failure or viral load non-suppressed	If DTG not used in the regimen	Switch to AZT+3TC + DTG
	If DTG used in the regimen	Switch to AZT + 3TC + PI/r
Viral load suppressed		Substitution to TLD regimen may be considered
Clinically/immunologically stable and VL unknown		Prioritize VL testing or consider programmatic / clinical indications for substitution to TLD
Clinically/immunologically stable on suboptimal first-line ARV regimens		Substitution to TLD
DTG in people living with HIV using second-line regimen		
Clinical/immunological failure or viral load non-suppressed		Switch to DTG (BD) + DRV/r (BD) ± NRTI

Current Status of Key ART Policies in 9 Countries

Country	Treat All	DTG Transition					Rapid ART initiation	Multi-month prescription (frequency)	Community ART implementation
		1st line	2nd line	3rd line	CC use in WCBA	VL in TLE stable (switching)			
CAM	✓	✓	×	✓	Any CC	✓	✓	3 MMP	countrywide
CDI	✓	✓	✓	✓	LA CC + Folate	✓	✓	3 & 6 MMP	3 MMP countrywide 6 MMP specific sites
MLW	✓	✓	×	✓	Informed choice	✓	✓	6 MMP	specific sites
MOZ	✓	✓	✓	×	LA CC + Folate	×	×	3 MMP	specific sites
NIG	✓	✓	✓	✓	LA CC	✓	✓	3 & 6 MMP	countrywide
TZN	✓	✓	✓	✓	Informed choice	×	✓	3 MMP	countrywide
UGN	✓	✓	✓	✓	Informed choice	✓	✓	3 & 6 MMP	countrywide
ZAM	✓	✓	✓	✓	Informed choice	✓	✓	6 MMP	countrywide
ZIM	✓	✓	✓	✓	Informed choice	✓	✓	3 & 6 MMP	countrywide

Nov 2019 (preliminary data)

Implementing DTG introduction/transition

- **Revise national guidelines according country context, considering clinical, epidemiological and programmatic factors**
- **Ensure adequate supply to meet anticipated demand (phased approach recommended)**
- **Ensure sufficient buffer stocks of older and new drugs throughout the transition period and beyond.**
- **Train health care workers**
- **Update registers and forms**
- **Implement active toxicity surveillance**
- **Appropriate communication/messaging to communities**

WHO ARV toxicity monitoring implementation tool and training materials

INSTI and new story of weight gain among PLHIV

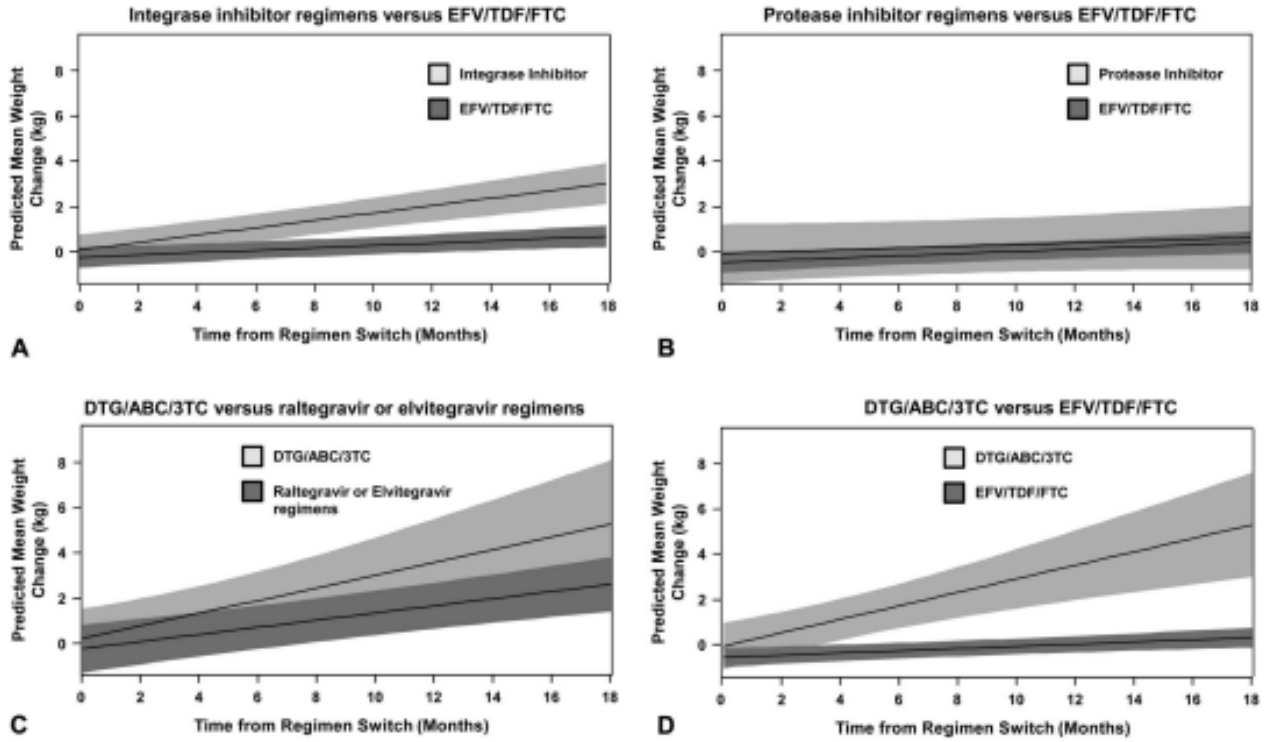
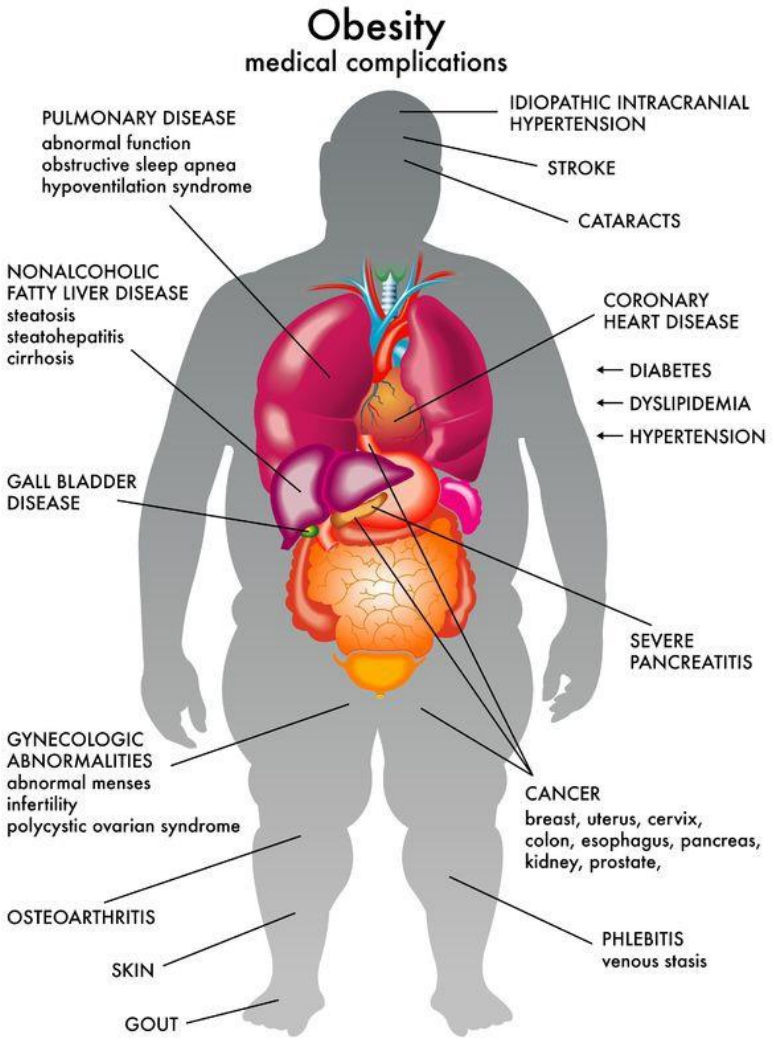


FIGURE 1. Weight change at 18 months among patients switching to an integrase inhibitor-based regimen versus remaining on EFV/TDF/FTC (panel A), switching to a protease inhibitor-based regimen versus remaining on EFV/TDF/FTC (panel B), switching to DTG/ABC/3TC versus a raltegravir or elvitegravir-based regimen (panel C), or switching to DTG/ABC/3TC versus remaining on EFV/TDF/FTC (panel D). Models adjusted for age, sex, race, total duration of ART, and baseline CD4⁺ T-cell count and weight.



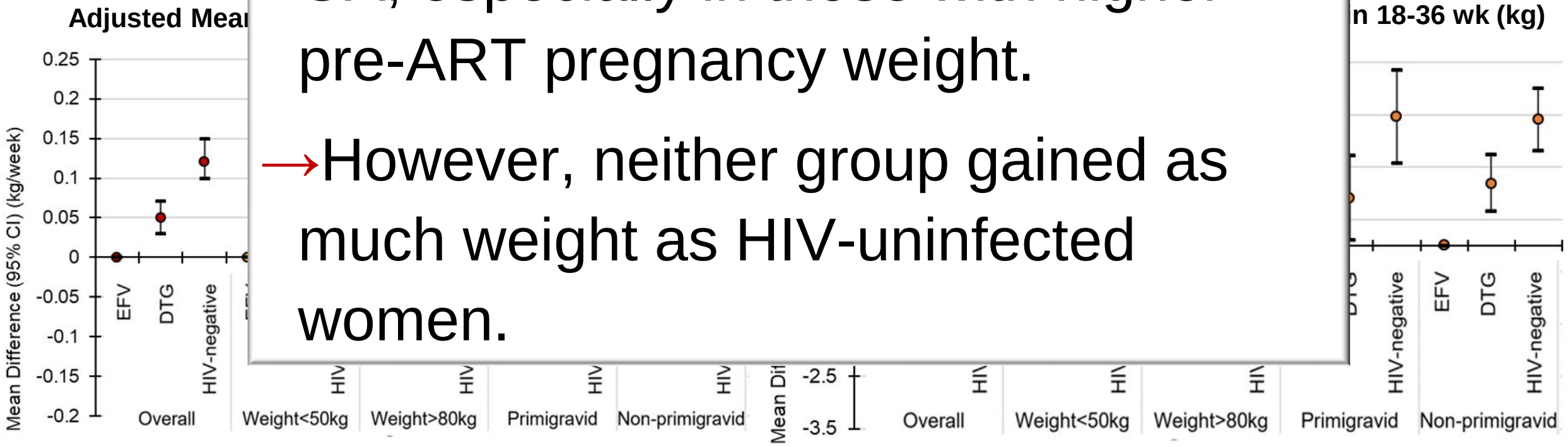
Weight Gain During Pregnancy in Women with HIV Starting DTG vs EFV vs Uninfected Women in Botswana, Tsepamo

Caniglia E et al. IAS July 2019, Mexico City Abs. LBPEB14

- Evaluated rate of weekly weight gain and weight gain between 18±2 to 36±2 wk GA
- Exposure g
  - HIV+ w
  - HIV+ w
  - HIV-uni

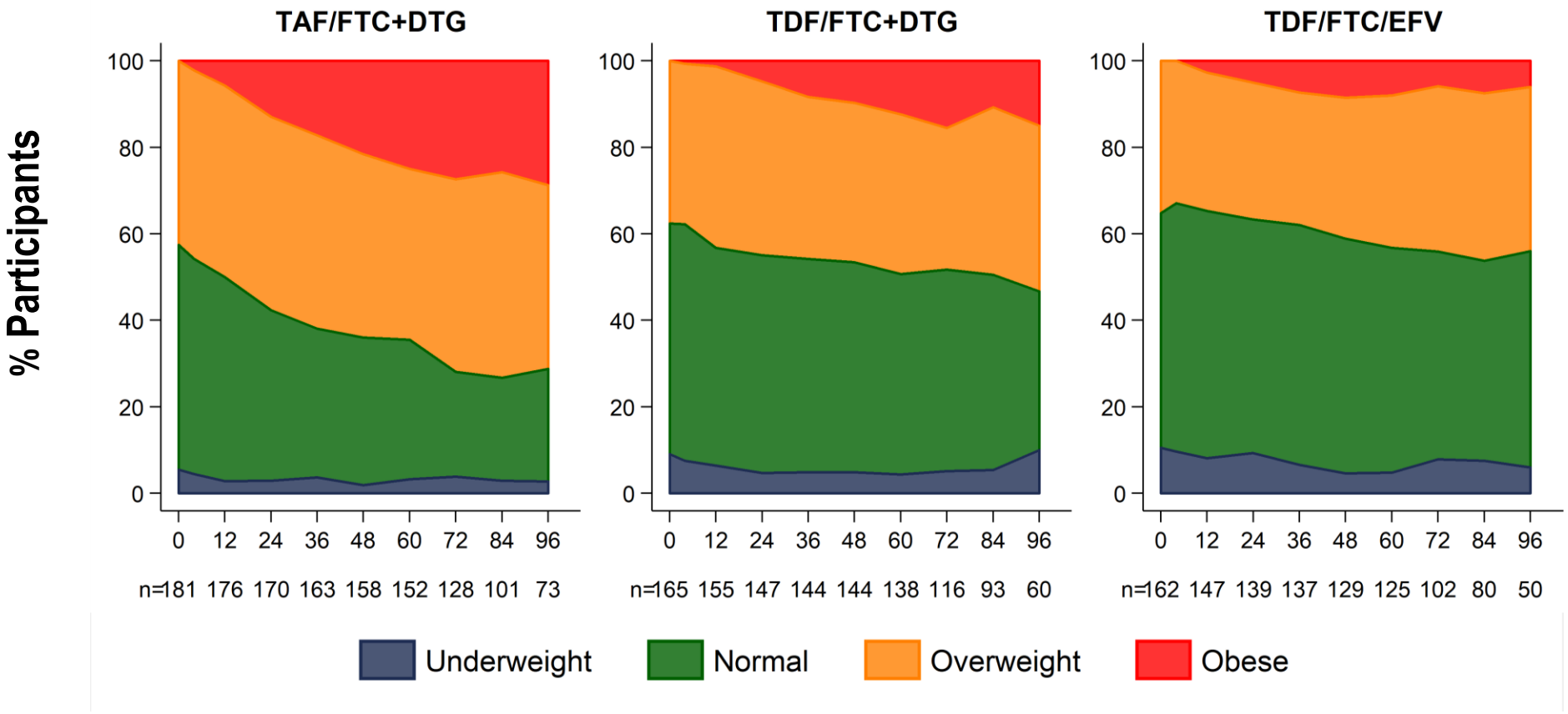
→Women initiating DTG compared to EFV gained more weight btn 18-36 wk GA, especially in those with higher pre-ART pregnancy weight.

→However, neither group gained as much weight as HIV-uninfected women.



Adjusted for: age, CD4, employment, education, parity, gravidity, marital status, site, smoking, alcohol, pre-pregnancy weight, weight at ART initiation (or first ANC), gestational age at ART initiation (or first ANC)

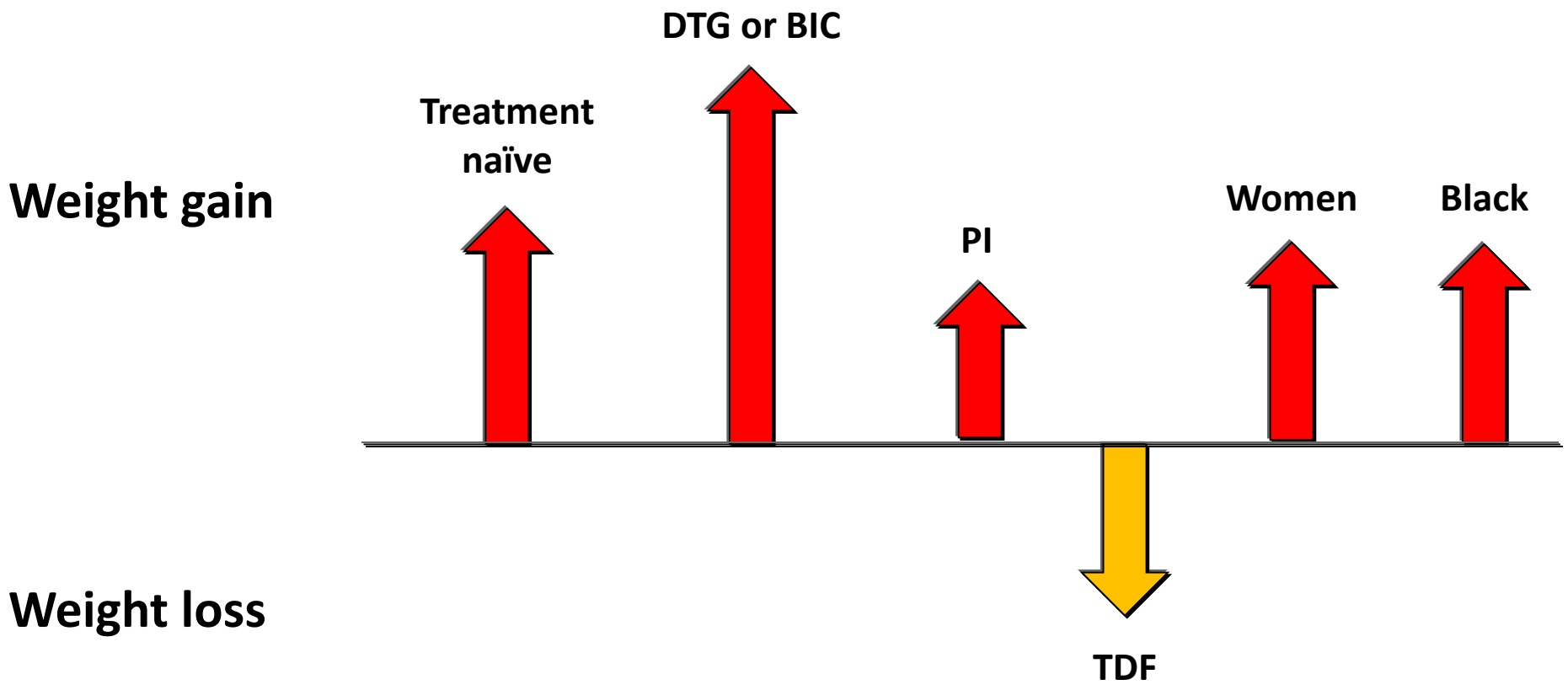
ADVANCE: BMI category over time: women (obese at baseline excluded)



Weight Gain with INSTIs (+ TAF?)

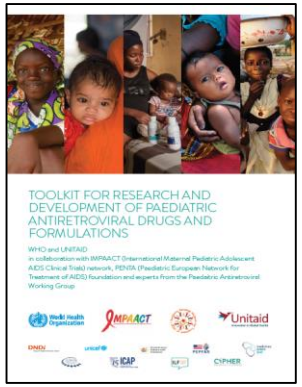
- **NAMSAL 48 weeks (baseline BMI 23)**
  - Significantly more weight/BMI gain & emergent obesity on TDF/3TC + DTG vs TDF/3TC/EFV400
- **ADVANCE 96 weeks (baseline BMI 22 in men, 27 in women)**
  - **TAF/F/DTG** vs **TDF/F/DTG** vs **TDF/FTC/EFV**
  - Men **+5kg**, **+4kg**, **+1kg** (DEXA: similar fat/lean mass gain)
  - Women **+10kg**, **+5kg**, **+3kg** (DEXA: fat>lean mass gain)

Drivers of weight gain/loss on ART



A Hill *et al*. Journal of Virus Eradication 2019

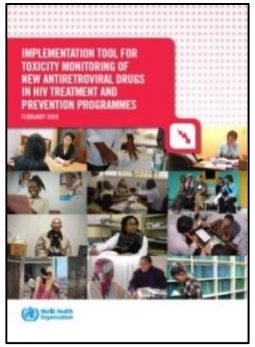
WHO support to countries for implementation of active toxicity monitoring and safe introduction of DTG and other new ARVs – guidance, tools and technical assistance

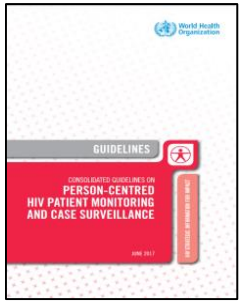


Toolkit with PV module for children

General population inc. children & adolescents

1. Guidance and tools inc. WHO ARV toxicity monitoring implementation tool and training materials

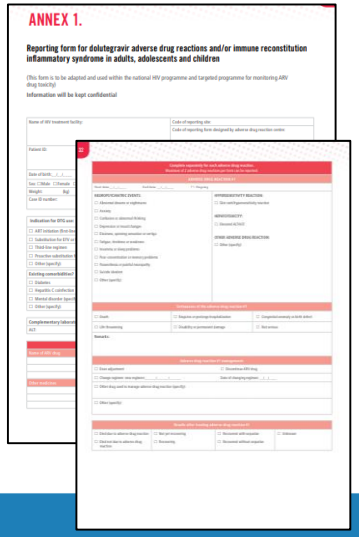




NEW

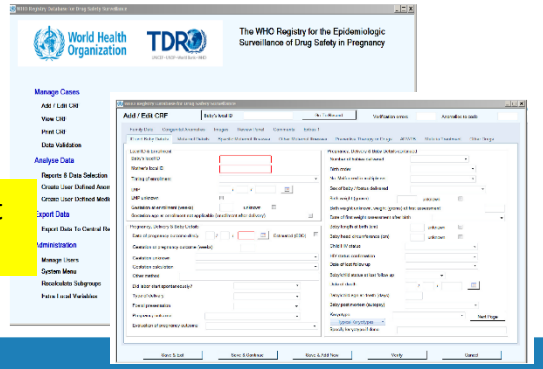
new indicators for toxicity in case surveillance & routine monitoring

Pregnant women



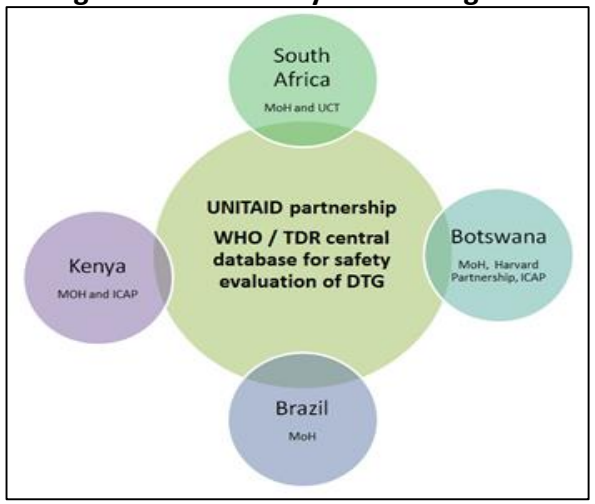
Generic DTG ADR notification form

Pregnancy & birth defect registry tools

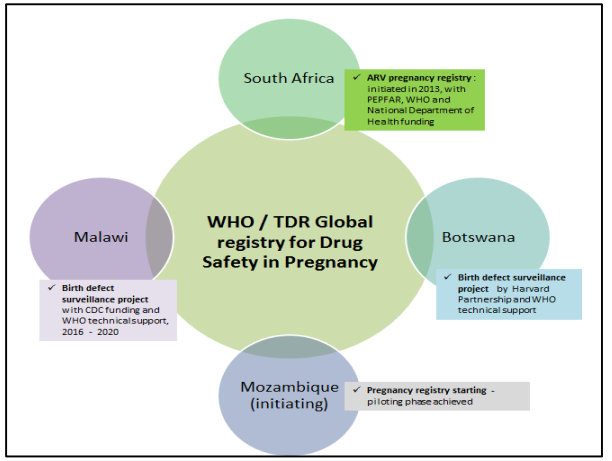


WHO global databases

WHO global ARV toxicity monitoring database

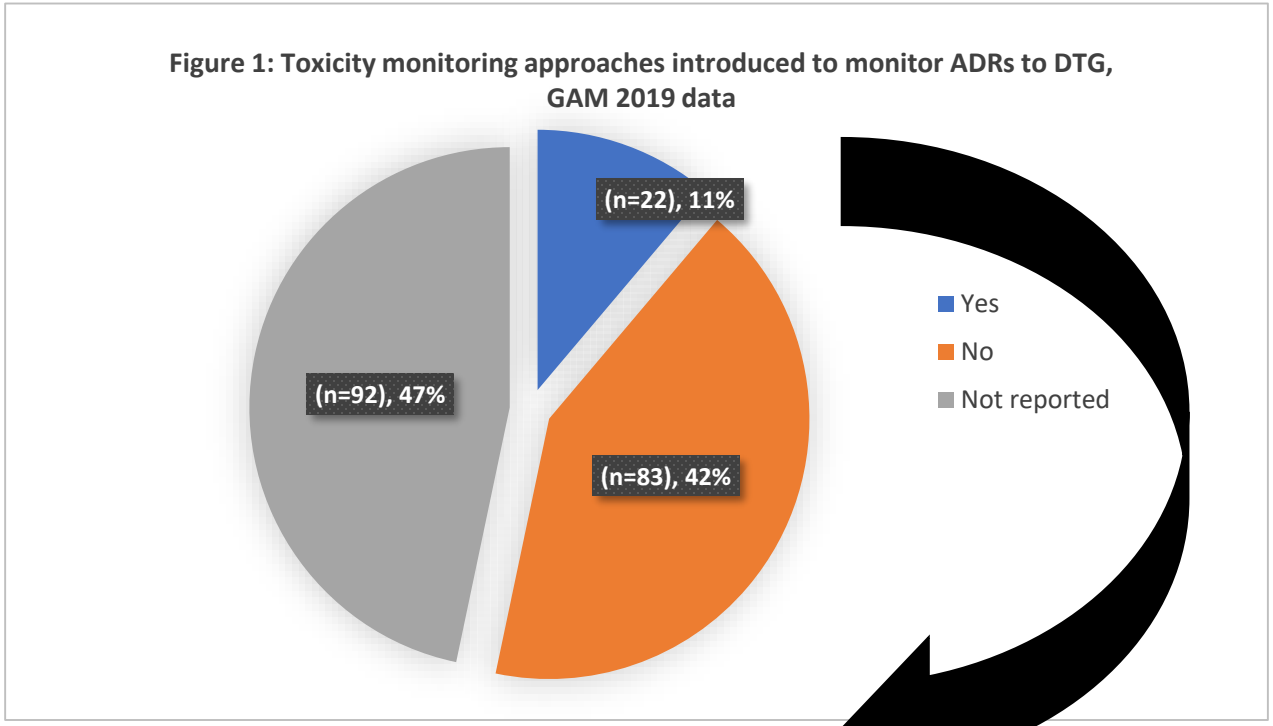


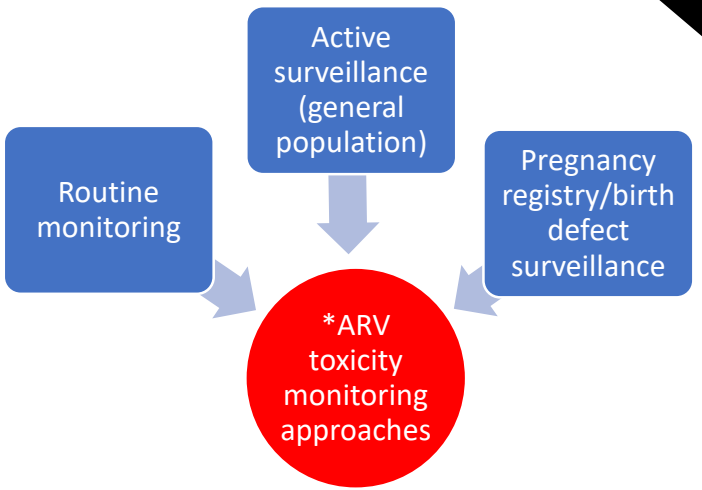
Central registry for drug safety in pregnancy



World Health Organization

Low proportion of countries reported specific policy on ARV toxicity monitoring or birth defect surveillance by HIV programmes by end 2018



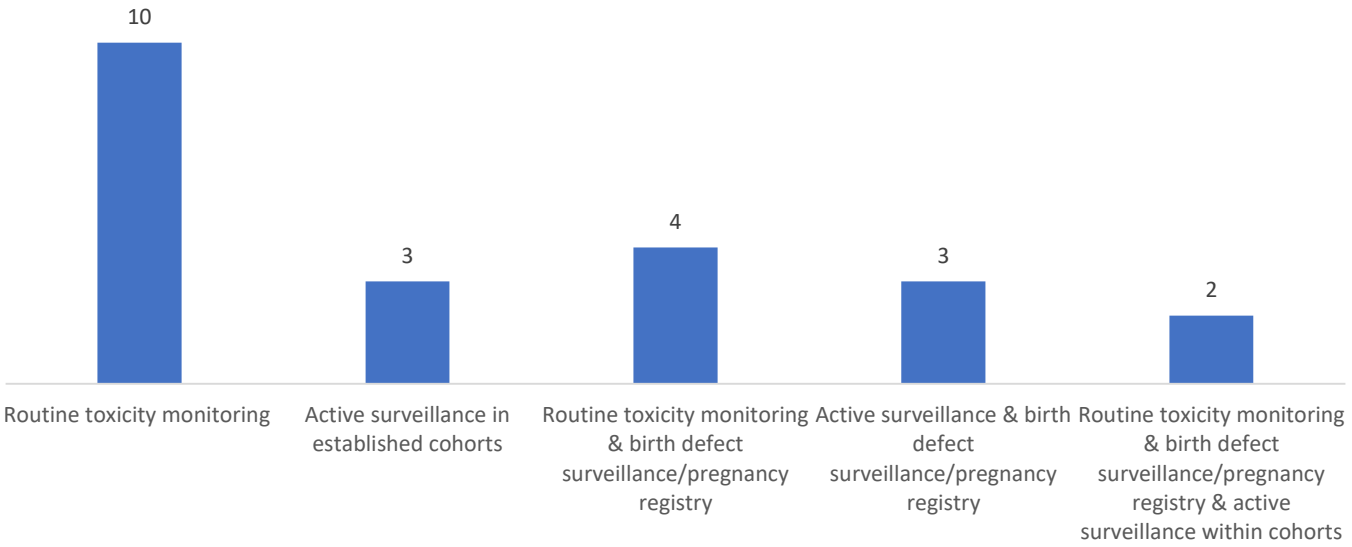


- N = 197
- Only 22 countries reported monitoring the toxicity of DTG
- How does it inform clinical management?
- HIV patient card updated, electronic medical records, DTG transition ?
- At what level of the health service ?
- Reporting of ADRs or trends remains limited

UNAIDS Global AIDS Monitoring Tool (GAM) 2018

…with the majority of them reported routine toxicity monitoring of DTG

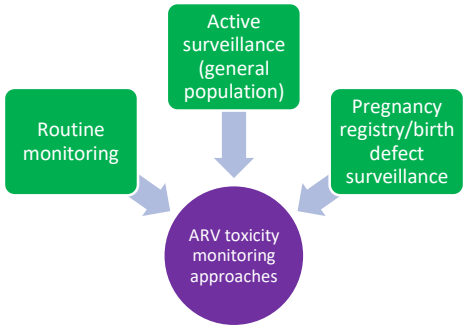
Figure 2: Type of toxicity monitoring approaches introducted ot monitor ADRs to DTG, GAM 2019 data



Majority of countries (18/37) reported monitoring ARV toxicity via routine HIV patient monitoring system

UNAIDS Global AIDS Monitoring Tool (GAM) 2018

- n = 22
- 16 countries routine monitoring for DTG
- 6 countries active toxicity monitoring/cohorts incl. Argentina, Eswatini, Malawi, Uganda, Mexico and Saudi Arabia
- 9 countries with pregnancy registry/BDS incl. DTG: Armenia, Botswana, Brazil, Iran, Malawi, Saudi Arabia, Uganda, Ukraine, Uruguay
- Brazil and Ukraine the 3 approches :

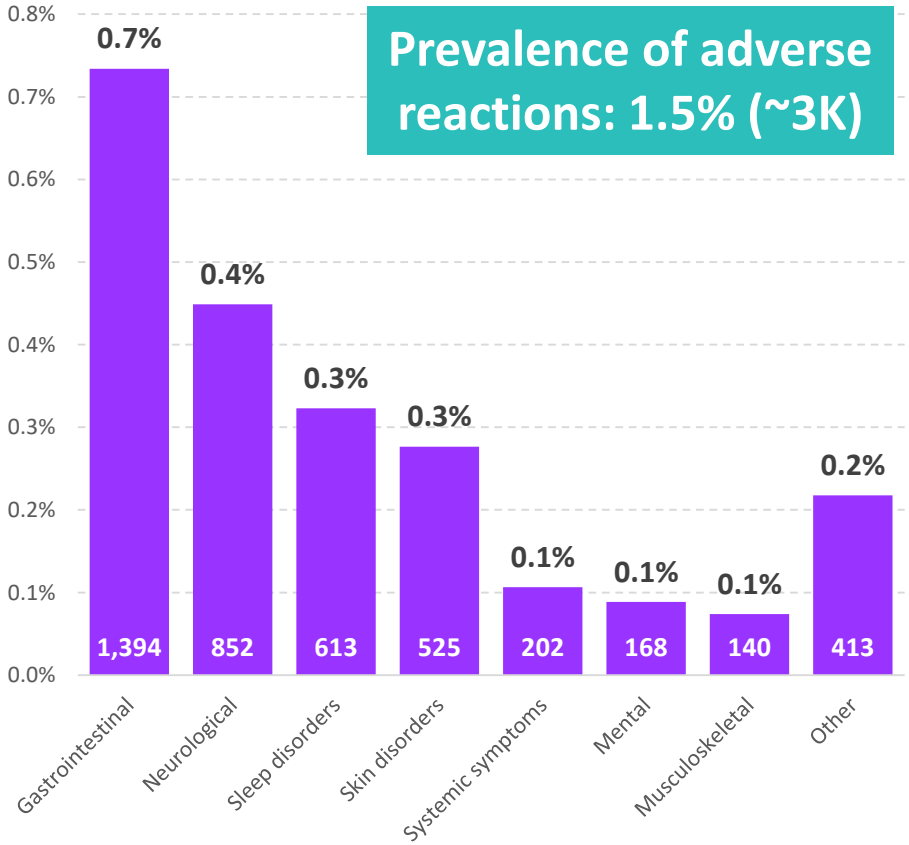


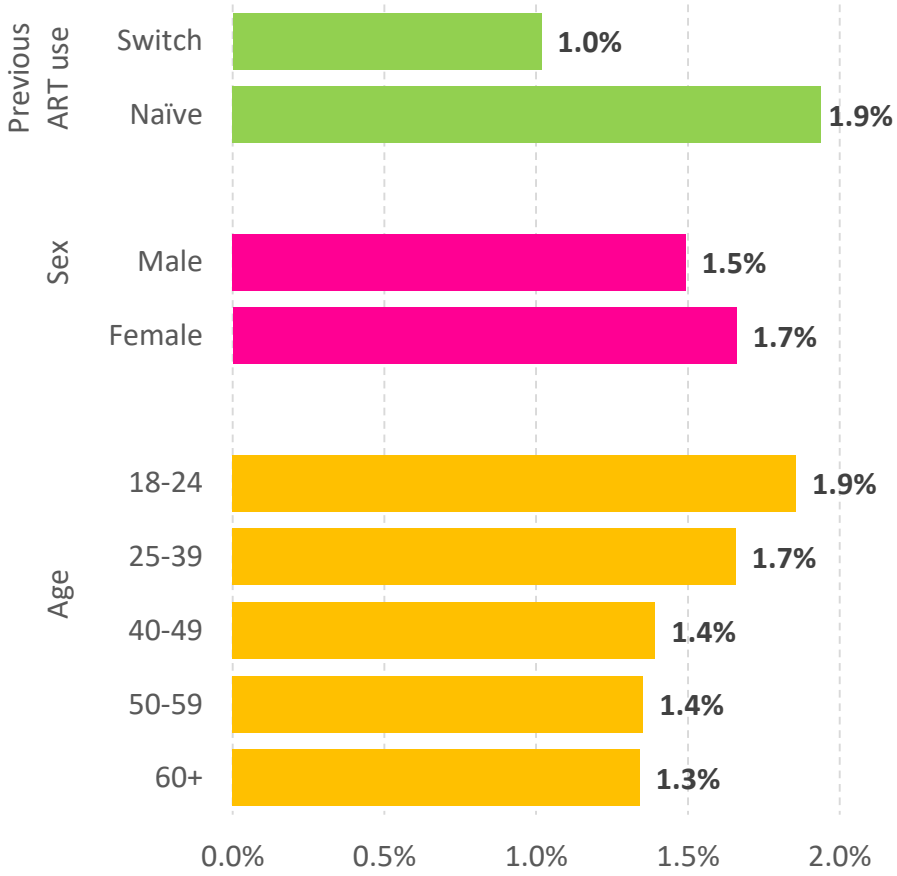
Brazilian experience on active pharmacovigilance of dolutegravir

- Active pharmacovigilance was implemented through patient interviews and a specific form was incorporated in the national ARV system
- Pharmacovigilance system coverage: 95% (190K/199K)


Medicine
OPEN
Observational Study
The Brazilian experience of implementing the active pharmacovigilance of dolutegravir
Abstract
1. Introduction

Batista et al. Medicine (2019) 98:10





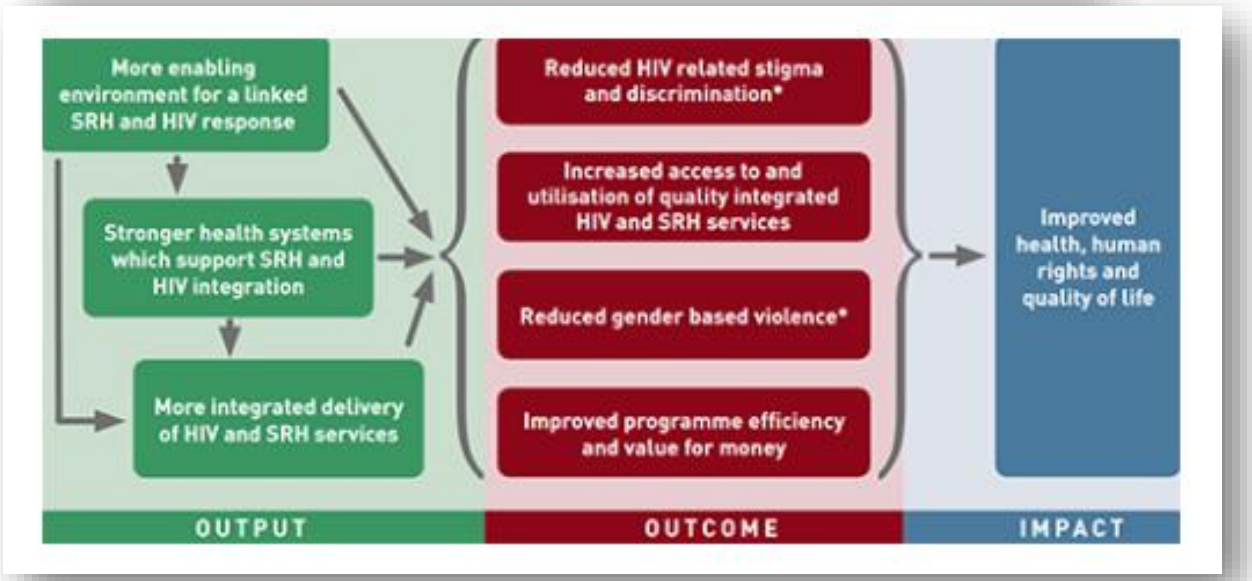
Sources: (1) Batista et al. The Brazilian experience of implementing the active pharmacovigilance of dolutegravir. Medicine (Baltimore). 2019 Mar;98(10):e14828.; and (2) Ministério da Saúde. Relatório de Monitoramento Clínico do HIV 2018 [Internet]. Available from: http://www.aids.gov.br/pt-br/pub/2018/relatorio-de-monitoramento-clinico-do-hiv-2018.

Main drug-drug interactions with DTG

Key drug interaction	Suggested management
Amiodaquine	Use an alternative antimalarial agent
Carbamazepine	Use DTG twice daily or substitute with an alternative anticonvulsant agent
Phenytoin and phenobarbital	Use an alternative anticonvulsant agent
Dofetilide	Use an alternative antiarrhythmic agent
Metformin	Limit daily dose of metformin to 1000mg when used with DTG & monitor glycemic control
Polyvalent cation products containing Al, Ca, Fe, Mg and Zn (eg: antacids, multivitamins & supplements)*	Use 2 hours before or 6 hours after DTG
Rifampicin	Use DTG twice daily or substitute with rifabutin

* There is no drug interaction of DTG with folic acid. However, folic acid is frequently included in multivitamin preparations which may also contain polyvalent cations.

World Health Organization



Programmes should strengthen the **integration of sexual and reproductive health services within HIV treatment** programmes to ensure reliable and consistent access to contraception for women and adolescent girls living with HIV.

2020 /21 Consolidated HIV Guidelines Timelines

Scoping Proposal Developed
Oct 2019

ICASA
Dec 2-8
WHO meetings

Evidence retrieval:
Systematic reviews
Values and preferences
Community consultations
Modelling
Nov 2019 – May 2020

Clinical GDG Meeting
May 2020

Key Clinical recommendations preview
July 2020

Share new clinical guidelines for

Operational / Service Delivery GDG Meeting
Sept 2020

Launch Full 2020 Consolidated HIV Guidelines
Dec 1 2020

Sep | Oct | Nov | Dec | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | Jan

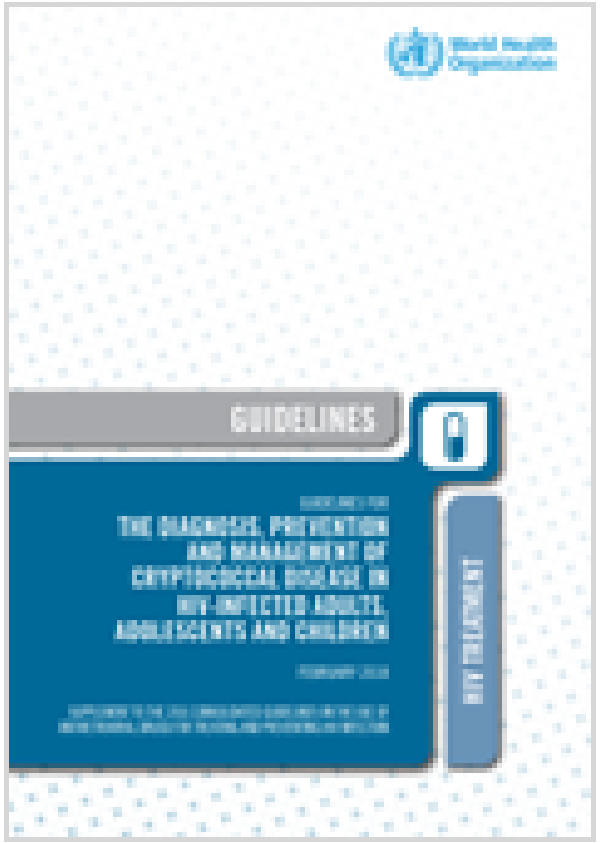
Community V&P Work

World Health Organization

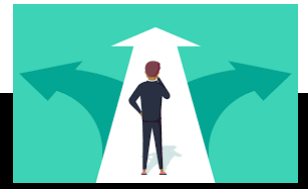
View to 2020/21 – Updating the Consolidated HIV Guidelines - Scoping for PICOs have started

Potential Cross-Cutting work

- Values and Preferences
- Community engagement
- Programmatic examples
- Good practice case studies



Future on ART Optimization: priorities and challenges



Potential priority	Challenges
Accelerate/consolidate TLD transition	• Long term safety (NTD and emerging AEs – body weight gain, metabolic syndrome) • Transition in stable patients (including those in 2nd line?) • Robustness in real life conditions and NRTI resistance (genetic barrier) • Support to transition plans • 3 MMD vs 6 MMD
Role of alternative regimens/drugs (TLE, PIs)	• How to guarantee adequate supply chain /availability
Accelerate the phase out of suboptimal drugs (eg: NVP)	• Removal from next EML ? • Support to accelerated phase out plans
Improve access to DRV	• Dose reduction and better formulations (FDCs, nanomedicines) • High cost as an important barrier • Would be better promote DRV/r in 2nd line or reserve it for 3rd line?
Role of TAF (should replace TDF?)	• Long term safety (body weight gain and other emerging AEs) • TB/HIV - is TAF dose adjustment a solution? • Transition in stable patients (all patients or only high risk groups?)
Dual therapy (including long acting drugs and emerging classes) in LMIC context	• What are the options in short, medium and long term? • Can we go beyond than simplification strategy? • Limited data on long term safety

CADO 3 drug list: short, medium and long term priorities

Short-term
1-2 years

- TDF/XTC/DTG
- TDF/3TC/EFV_{400}
- DRV/r (400/50mg)

Medium-term*
2-5 years

- TAF/XTC
- TAF/XTC/DTG
- new DRV/r formulations §

Long-term
+5 years

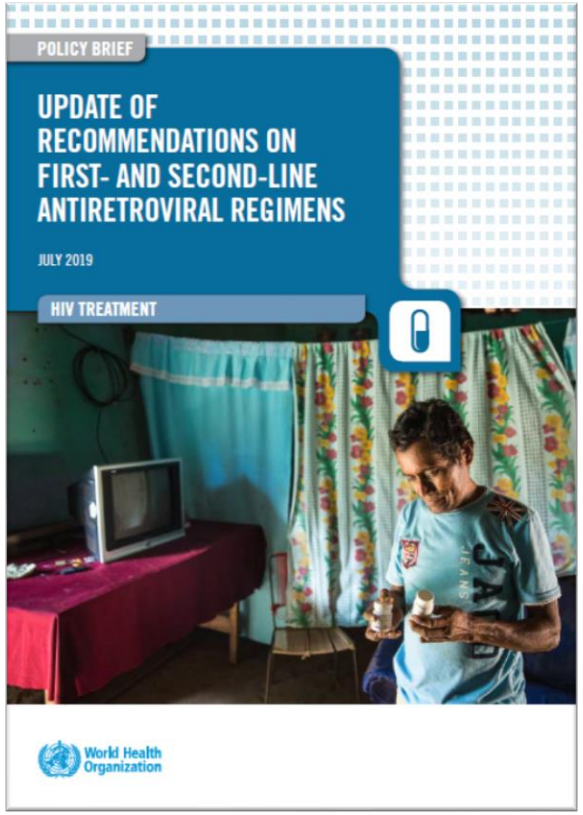
- Long acting formulations (entry inhibitors and INSTIs)
- maturation & capsid inhibitors
- bNAbs

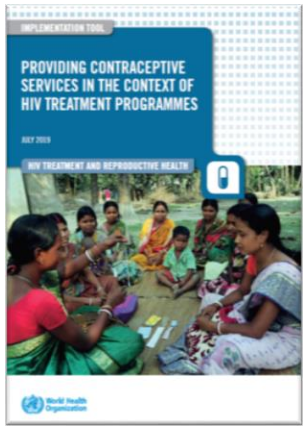
* Other lower priority products can be consider if new data become available in the future (bictegravir, dorevirine, DTG/3TC, DRVr/3TC, DTG/DRV/r)
§ Low dose standard formulation (400/100mg) or standard dose nanoformulation (800/100 mg)

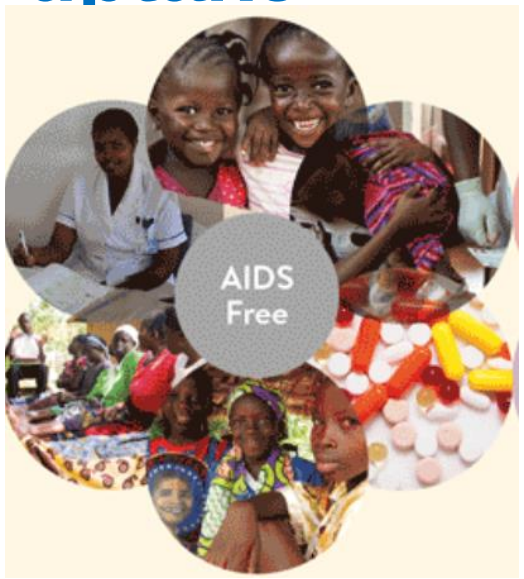
https://www.who.int/hiv/pub/meetingreports/cado3-arv-optimization/en/

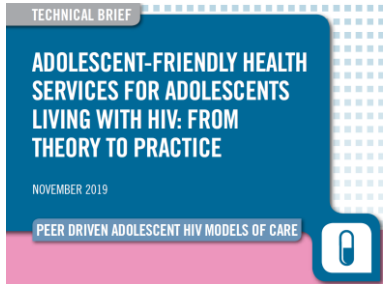
World Health Organization

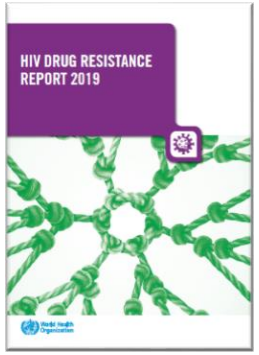
WHO documents in 2019 to support guideline uptake











https://www.who.int/hiv/en/

https://www.who.int/hiv/pub/en/

New WHO HIV Tx App
Get online with WHO ARV and Treatment Guidelines - 2019

- https://hivtx.org
- https://hivtx.org/iphone
- https://hivtx.org/android

- This is a Beta Launch-- We want your feedback!

Acknowledgements

All members Guidelines Development Group members

- Elaine Abrams & Serge Eholie
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- Francoise Renaud
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- Silvia Bertagnolio
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- Ajay Rangaraj
- Anisa Ghadrshenasa

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- **AFROCAB, iBASE, ITPC, Salamander Trust, ICW, GPN+, APN+**

World Health Organization

ART Optimization Programme Advisory Committee (PAC) Outbrief for Industry

November 26, 2019
Washington, DC

What is the PAC?

ART Optimization Programme Advisory Committee Meeting

- Provide **expert input** on how to strengthen efforts to accelerate the introduction of better HIV treatment through the ART optimization programmes
- Provide an objective a**ppraisal of progress** based on programme's goals and milestones
- Promote **alignment of ART optimization with global efforts on ART simplification and optimization**

2019 PAC Meeting

Oct. 3-4, Geneva, Switzerland

Co-Chairs of PAC	
Name	Organization
Martin Auton	Global Fund
Meg Doherty	World Health Organization
Experts Providing Recommendations	
Jacqueline Wambui	Health Gap / National Empowerment Network of People Living with HIV/AIDS in Kenya (NEPHAK)
George Siberry	USAID
Luckyboy Mkhondwane	Treatment Action Campaign
Francoise Renaud	World Health Organization
Marco Vitoria	World Health Organization
Nathan Ford	World Health Organization
Martina Penazzato	World Health Organization
Polly Clayden	HIV i-Base
Andrew Hill	University of Liverpool

ART Optimization Program FUNDING Agencies	
Katherine Blumer	Unitaid
Danielle Ferris	Unitaid
Carmen Perez Casas	Unitaid
Denitza Andjelic	Unitaid
Tim Ryan	Unitaid
Emily Harris	USAID
Messai Belayneh	USAID / Supply Chain
Mary Catharine McKeithen	USAID
Julia Martin	USG/State Department

Implementer Organizations	
Name	Organization
Caroline Middlecote	Clinton Health Access Initiative
Polly Clayden	HIV i-Base
Eric Delaporte	IRD
Nicola Loffredi	Medicines Patent Pool
Hannah Moak	Medicines Patent Pool
Sandra Nobre	Medicines Patent Pool
Michelle Moorhouse	Wits RHI - Ezintsha
Saye Khoo	University of Liverpool
Andrew Hill	University of Liverpool
Andrew Owen	University of Liverpool
Steve Rannard	University of Liverpool
Mark Polizzotto	University of New South Wales
Isabelle Andrieux- Meyer	DNDi
Celicia Serenata	Wits THI
Maureen Syowai	ICAP at Columbia University
Jen Cohn	EGPAF
Trevor Crowell	AFRICOS
Alexandra Calmy	HUG
Eugene Choi	Medicines for All Institute
Tim Cressey	Stellenbosch University
Helen Rabie	Stellenbosch University
Hiwot Haile-Selassie	WHO
Imelda Mahaka	PZAT
Annette Reinisch	Global Fund
Jinkou Zhao	Global Fund
Pablo Rojo	PENTA
Kenly Sikwese	AfroCAB

2019 ART Optimization Landscape

Key Questions

- Safety of TAF periconception and pregnancy
- Changes in body weight in a range of studies of DTG combined with either TDF or TAF (to validate results from ADVANCE)
- Outcomes from switching from TLE to TLD without viral load
- Safety and efficacy in young children

Summary of PAC Research Priority Topics being Addressed in **ADULT CLINICAL TRIALS**

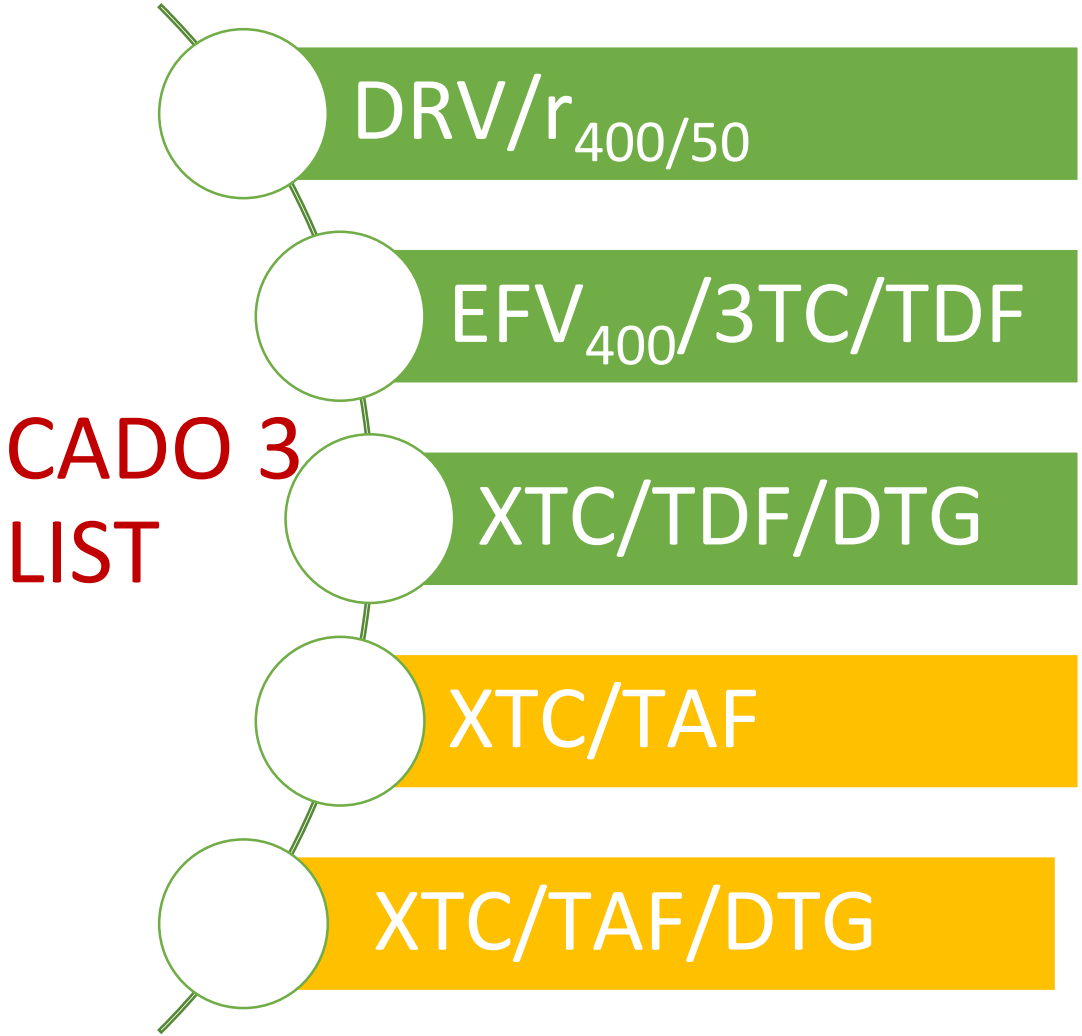
PAC research priority topic	NAMSAL	ADVANCE	VESTED	VISEND	NADIA	ARTIST	D2EFT	DOLPHIN 2
Safety of DTG and TAF periconception and pregnancy**(3)**			✓					✓
Changes in body weight/cardiometabolic risk with DTG combined with TAF or TDF **(1), (2)**	✓	✓	✓	✓	✓	✓	✓	✓
Outcomes from switching from TLE to TLD w/o VL (**1)(2)**						✓	✓	
Safety and efficacy of DTG and TAF in adolescents	✓	✓	✓	✓	✓	✓	✓	✓
Expected timeline	Long term follow up to 2021	Completion by Q1 2020	Primary completion July 2020	Start Q 2/3 2019	Primary completion Dec. 2020	Awaiting SAHPRA approval	Primary completion Dec. 2020	Primary completion Q4 2021

Adult Observational Studies also contributing: (1) AFRICOS, (2) ObserveTLD, (3) Tsepamo

Implementing DTG introduction/transition

- **Revise national guidelines according country context, considering clinical, epidemiological and programmatic factors**
- **Ensure adequate supply to meet anticipated demand (phased approach recommended)**
- **Ensure sufficient buffer stocks of older and new drugs throughout the transition period and beyond.**
- **Train health care workers**
- **Update registers and forms**
- **Implement active toxicity surveillance**
- **Appropriate communication/messaging to com**

WHO ARV toxicity monitoring implementation tool and training materials



DRVr (400/50 mg): heat stable boosted formulation to optimize PI options in 2nd line (pill size)

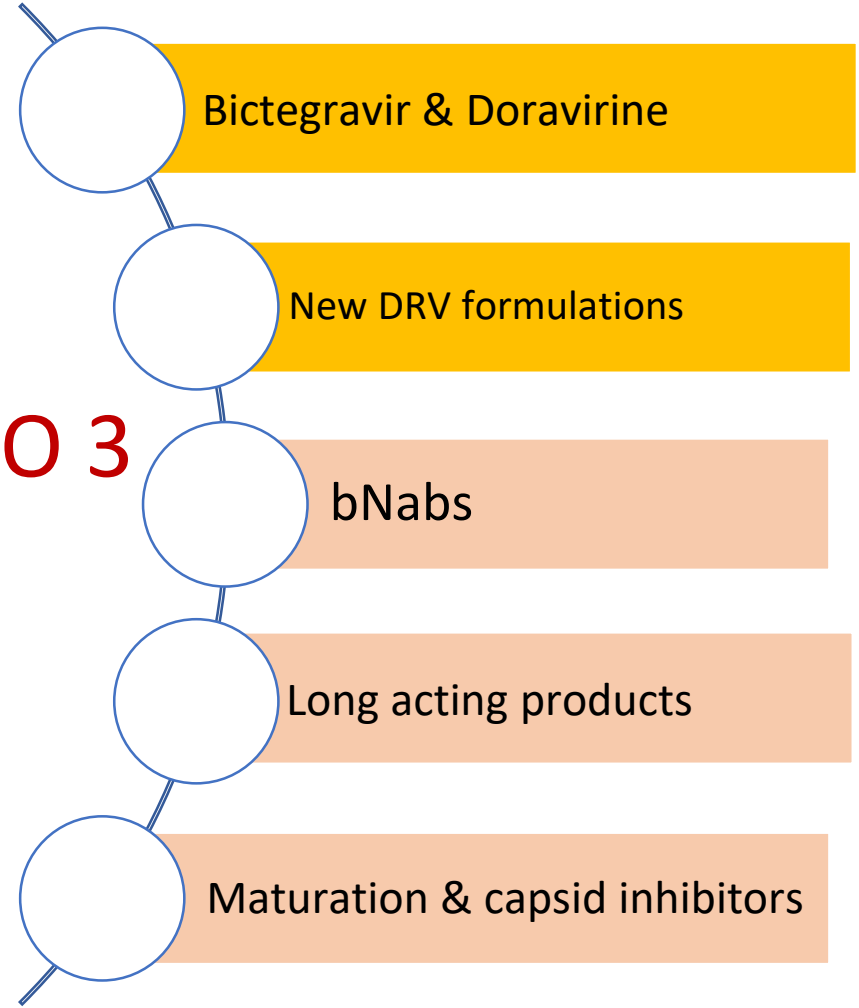
EFV400/3TC/TDF: alternative regimen for those that cannot use DTG-based regimens (better tolerability than EFV600)

XTC/TDF/DTG critical FDC to provide short term expansion of DTG as preferred first line.

XTC/TAF and XTC/TAF/DTG: Desirable for full harmonization with children but some gaps remain (TAF safety /efficacy studies in PW and dose in TB coinfection still ongoing).

World Health Organization

CADO 3 LIST



Bictegravir and **Doravirine:** Can be a "plan B" due DTG unexpected findings. However, very limited data in PW, TB at this stage.

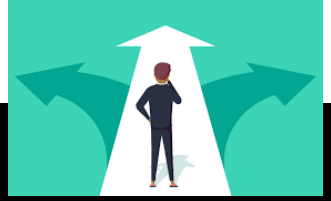
New DRV formulations: Includes lower doses of standard formulations or nano-formulations.

bNabs: Good potential as prevention and as co-treatment with ARVs , for enhancing HIV-specific immune response, and reduction of HIV reservoir.

Long Acting Agents: Current formulations (i.e. CAB/RPV) is being studied and show promising. Could represent a suitable opportunity for HIV prevention and treatment in some populations.

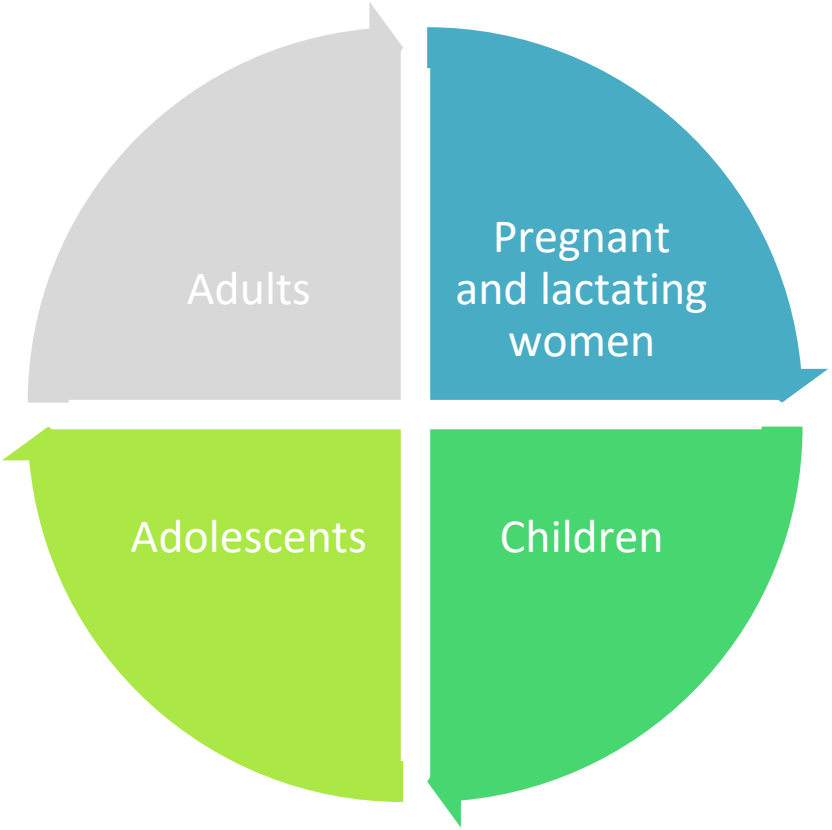
Maturation & capsid inhibitors: considered of interest in long term (long acting products), active review of investigation plans is encouraged as more data from phase I/II studies become available

ADULT ART: priorities and challenges



Potential priority	Challenges
Accelerate TLD transition	• Long term safety (NTD and emerging AEs) • Transition in stable patients (including those in 2nd line?) • Robustness in real life conditions and NRTI resistance (genetic barrier) • Support to transition plans
Role of alternative regimens/drugs (TLE, PIs)	• How to guarantee adequate supply chain /availability
Accelerate the phase out of suboptimal drugs (eg: NVP)	• Remove from next EML ? • Support to phase out plans
Improve access to DRV	• Dose reduction and better formulations (FDCs, nanomedicines • High cost is also an important barrier • Better promote it in 2nd line or reserve for 3rd line?
Role of TAF (should replace TDF?)	• Long term safety (body weight gain and emerging AEs) • TB/HIV - is dose adjustment a solution? • Transition in stable patients (all or only high risk groups?) • Include in EoI ???
Dual therapy (including long acting drugs and emerging classes)	• What are the options in short , medium and long term? • Can we go beyond than simplification strategy? • Limited data on long term safety

PADO4: expanding the scope to address the full life-cycle and its specificities



Clinical Trial Drug Development Phases, with Focus on Drugs That Will Be Used in Pregnancy

	PHASE I	PHASE IIa	PHASE IIb	PHASE III	PHASE IV
Non-Pregnant	Pharmacokinetics, safety, tolerability	Pharmaco-dynamics, dose range	Definitive dose, efficacy	Efficacy, comparison to standard of care	Post-market approval surveillance, safety, rare events
Pregnant, Current Status of Studies	Not included	Not included	Not included	Generally not included; if woman becomes pregnant, stops drug, often comes off study	Phase I pregnancy study may or may not be done; post-market safety surveillance may or may not be done
Pregnant, Proposed Status of Studies	**Not included →exception: life-threatening conditions with no treatment available (e.g., Ebola)**	**Not included →exception: life-threatening conditions with no treatment available (e.g., Ebola)**	**Phase I in parallel to phase IIb in pregnant women with limited options and hence favorable benefit/risk**	**→If phase I during phase IIb, enroll into phase III trials →If phase I not done, phase I in parallel to or as substudy of phase III →Once safe dose, enroll in phase III trials**	**→If phase I <u>not</u> done and drug will be used in pregnancy, do phase I →If have phase I data, potential comparison to standard regimen used in pregnancy (safety)**

World Health Organization

Introducing DTG for children and adolescents

DTG adoption for Paediatric 1st line

In January 2019, the WHO-convened Paediatric ARV Working group reviewed data from the ODYSSEY trial and formally endorsed the use of **50 mg film-coated tablets for all children above 20 kg.**

FIVE common challenges

- Access to SRH services limited
- Age of consent policies limit access
- Limited supplies of contraceptives
- Information on DTG use not adolescent friendly
- Cultural norms that stigmatize use of contraceptives

As of September 2019, 21 of the 21 priority countries for paediatric HIV have adopted DTG for children and it's estimated that about 500,000 children can now start or transition to a more durable ART regimen

World Health Organization

PK of DTG 5 mg Dispersible Tablets in Children 6-<20 Kg

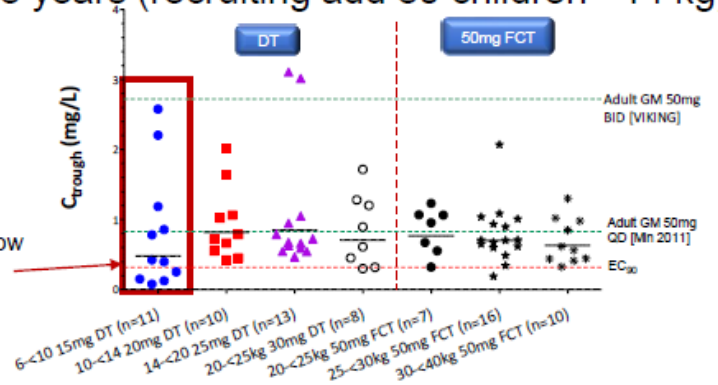
Waalewijn H et al. IAS July 2019, Mexico City Abs. WEAB0401LB

- ODYSSEY is a randomised, non-inferiority trial evaluating efficacy and safety of 1st and 2nd line DTG ART vs standard of care in 700 HIV-infected children <18 years (recruiting add 80 children <14 kg)

WHO Weight bands, kg	DTG DT* once daily (# tablets, daily dose, mg)
3 to <6 (<6 months old)	(5mg)
3 to <6 (>6 months old)	2 (10mg)
6 to <10	3 (15mg)
10 to <14	4 (20mg)
14 to <20	5 (25mg)
20 to <25	6 (30mg)

*DTG dispersible tablet (DT) formulation; DT are ~1.6 to 2.0x more bioavailable than film coated tablets (FCT)

- 4/11 (36%) had C_{trough} values below EC_{90} (0.32 mg/L)



		ODYSSEY Weight Bands			Reference adults	
WHO weight band		6-<10	10-<14	14-<20	≥ 40kg	≥ 40kg
Dose	mg/formulation	15 DT	20 DT	25 DT	50 FCT QD*	50 FCT BID**
N		11	10	13	10[a]	24[b]
Dose/weight (range)	mg/kg	1.8 (1.5-2.2)	1.8 (1.6-2.0)	1.4 (1.3-1.7)	-	-
C_{trough} (CV%)	mg/L	0.48 (167)	0.82 (55)	0.85 (67)	0.83 (26)[a]	2.72 (70)[b]
AUC_{0-24h} (CV%)	mg*h/L	49.3 (77)	77.0 (22)	69.5 (30)	43.4 (20)[a]	93.4 (50)[b]
C_{max} (CV%)	mg/L	5.4 (50)	8.0 (22)	7.1 (21)	3.3 (16)[a]	5.4 (40)[b]

PK expressed as geometric mean with coefficient of variation (%), and median (range) for dose/weight. FCT, film-coated tab; DT, dispersible tab
[a]Fasted HIV-positive adults. [b]HIV-positive treatment experienced adults, fed state not specified.

- C_{trough} low in 6-<10kg weight band
- AUC inbetween adult QD and BID
- C_{max} somewhat higher than adult in higher weight bands (10-<20)

How is the Ped ARV landscape expected to change?

DTG 50mg and TLD already available

Facilitated intro of RAL granules for infected neonates

Implementation guidance, tools and resources will be available for countries implementing birth testing

Increased capacity for LPV/r pellets/granules → *Supply is less of a constraint*

ABC/3TC/LPV/r "4 in 1"

FILED → SRA Approval ~ 6 mos → ~ 6 mos → Availability in country

DTG 5mg disp tablet

All P1093 cohorts (4 wks and up)

Anticipated filing → SRA Approval ~ 6 mos → ~ 6 mos → Availability in country

DTG 10mg scored disp tab

Anticipated filing → SRA Approval ~ 6 mos → ~ 6 mos → Availability in country

PADO list evolution

PADO 1-2013	PADO 2-2014	PADO 3-2016	PADO 4-2018
LPVr 4-in-1	LPVr 4-in-1 (30/15/40/10 mg)*	In advanced development	
ABC/3TC/EFV	ABC/3TC/EFV (150/75/150 mg)*	In advanced development	
ATVr	ATVr (100/33mg)*	Removed§	
NVP 20 mg	NVP/AZT	NVP/AZT	Removed
RAL	RAL	RAL (50 mg scored)*	Removed
DRVr	DRVr	DRVr (120/20 mg)*	DRVr (120/20 mg)
DTG single	DTG paeds single	DTG paeds single (5 mg)*	DTG paeds single (10 mg scored) dispers tab
DTG/3TC/ABC	DTG/3TC/ABC	DTG/3TC/ABC (5/30/60 mg)*	DTG/3TC/ABC (5/30/60 mg) dispersible tab
F/TAF	F/TAF	F/TAF	XTC/TAF dispersible tablets
DTG/XTC/TAF	DTG/XTC/TAF	DTG/XTC/TAF	DTG/XTC/TAF dispersible tablets
		DTG/DRVr	Removed
		DTG/3TC	Removed
		LA	MK 8591
		bNab	Doravirine
			LA
			bNab
			New delivery technologies

Summary of gaps and the trials/studies to answer them

Questions /Side Effects /ADRs	Current Trial Data	Results from extended or new trials to help answer
NTD - Longer term outcomes	TSEPAMO, APR, Enhanced Toxicity Monitoring	TSEPAMO Active Surveillance, Kenya, Uganda, Brazil, Malawi, S Africa
Weight gain - Role DTG /INSTI - Role of TAF - Background obesity rates	ADVANCE, Namsal, Vital records	ADVANCE, NAMSAL, ViiV, Gilead, Expanded active surveillance
Hyperglycemia - Role of DTG - Role of other ARVs	No RCT, Uganda case series	ADVANCE, NAMSAL, DAWNING, DEFT, NIH Study
Erectile Dysfunction	No Data in 2019	As above
Switching to DTG when stable on EFV	No data in 2019	DEFT, Observe TLD

Trials Underway to Evaluate 6-month Multi-Month Dispensing (MMD)

All trials are expected to be completed (for primary outcomes) by late 2019

Fatti et al. Trials (2018) 19:79
DOI 10.1186/s13063-018-2469-y

Trials

STUDY PROTOCOL Open Access

The effectiveness and cost-effectiveness of 3- vs. 6-monthly dispensing of antiretroviral treatment (ART) for stable HIV patients in community ART-refill groups in Zimbabwe: study protocol for a pragmatic, cluster-randomized trial

Geoffrey Fatti[1*], Nicoletta Ngorima-Mabhena[2], Frank Chirowa[2], Benson Chirwa[2], Kudakwashe Takarinda[3,4], Taurayi A. Tafuma[5], Nyikadzino Mahachi[5], Rudo Chikodzore[6], Simon Nyadundu[7], Charles A. Ajayi[8], Tsitsi Mutasa-Apollo[4,9], Owen Mugurungi[4], Eula Mothibi[1], Risa M. Hoffman[10] and Ashraf Grimwood[1]

Wilkinson et al. BMC Infectious Diseases (2019) 19:674
https://doi.org/10.1186/s12879-019-4287-6

BMC Infectious Diseases

South Africa

STUDY PROTOCOL Open Access

A cluster randomized controlled trial of extending ART refill intervals to six-monthly for anti-retroviral adherence clubs

Lynne Wilkinson[1], Anna Grimsrud[2], Tali Cassidy[3,4*], Catherine Orrell[5,6], Jacqueline Voget[7], Helen Hayes[7], Claire Keene[3], Sarah Jane Steele[3] and Rodd Gerstenhaber[3]

Hoffman et al. Trials (2017) 18:476
DOI 10.1186/s13063-017-2177-z

Trials

Malawi & Zambia

STUDY PROTOCOL Open Access

Varying intervals of antiretroviral medication dispensing to improve outcomes for HIV patients (The INTERVAL Study): study protocol for a randomized controlled trial

Risa Hoffman[1,2*], Ashley Bardon[1,2], Sydney Rosen[2,3,4], Matthew Fox[2,5], Thoko Kalua[6], Thembi Xulu[2,7], Angela Taylor[7,8] and Ian Sanne[2,7,9]

Faturiyele et al. BMC Public Health (2018) 18:1069
https://doi.org/10.1186/s12889-018-5961-0

BMC Public Health

STUDY PROTOCOL Open Access

Outcomes of community-based differentiated models of multi-month dispensing of antiretroviral medication among stable HIV-infected patients in Lesotho: a cluster randomised non-inferiority trial protocol

I. O. Faturiyele[1], T. Appolinare[2], N. Ngorima-Mabhena[3], G. Fatti[4,5], I. Tshabalala[6], V. J. Tukei[7] and P. T. Pisa[8*]

Excellent Outcomes for 6-Month MMD

IAS 2019

LBPED36

Twelve-month retention and viral load outcomes from a non-inferiority cluster randomized trial extending adherence club ART refill dispensing intervals to 6-monthly

SOUTH AFRICA

Keitu Lebelo[1], Tali Cassidy[1,2], Anna Grimsrud[3], Claire Keene[1], Sibusiso Ndlovu[1], Helen Hayes[4], Catherine Orrell[5,6], Nompumelelo Zokufa[1], Tabitha Mutseyekwa[1], Jacqueline Voget[4], Rodd Gerstenhaber[1], Lynne Wilkinson[7]

1 Medécins Sans Frontières, Khayelitsha, South Africa; 2 Department of Public Health Medicine, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa; 3 International AIDS Society, Cape Town, South Africa; 4 Western Cape Government Department of Health, Cape Town, South Africa; 5 Department of Medicine, Faculty of Health Sciences, Cape Town, South Africa; 6 The Desmond Tutu HIV Centre, Institute for Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa; 7 Center for Infectious Disease and Epidemiological Research, School of Public Health and Family Medicine, University of Cape Town

Corresponding author: Dr Claire Keene; msfocb-khayelitsha-hivmam@brussels.msf.org

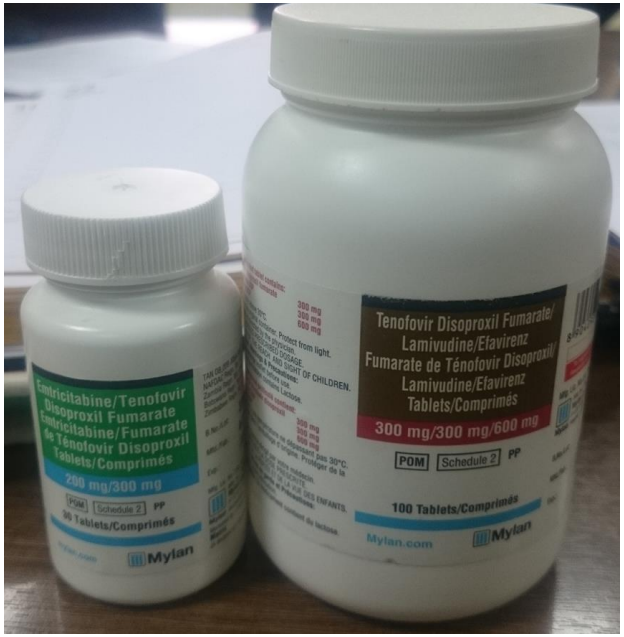
12-month outcomes	Standard of care AC	Intervention AC (Six-month refills)	p-value
Retention in care	98% (97.2-98.8)	97% (96.1-98.2)	0.252
Retention in club care	83% (80.4-84.9)	86% (83.5-87.9)	0.186
Viral Load completion	94.4% (92.9-95.7)	98.0% (96.9-98.8)	0.06
Viral Load suppression	96.5% (95.2-97.4)	97.8% (96.7-98.8)	0.11

In cluster randomized trial, comparable and excellent 12-month Retention, Viral load coverage, and Viral load suppression outcomes with 6-month ART refills compared to 2-month ART refills in adherence club (AC) ART refill model.

Promoting MMD with 90- and 180-day pill bottle sizes

- Tripling (or sextupling) the pill count and number of days' supply *doesn't* triple (or sextuple) the size of the bottle
- Potential for greater client convenience and reduced storage/shipping/packaging costs

Gaining Packaging Efficiencies



Opportunity for standardized packaging and presentation across manufacturers for the same ARVs?

Summary of 2019 PAC Recommendations

- **Support continued scale-up of existing treatment education, including refining audience-specific communication materials, approaches and products**
- **Share and interrogate data – country experiences & cross-trial analyses – to better understand changes in weight gain associated with DTG, TDF and TAF**
- **As TLD uptake increases, leverage programmatic data sources to complement clinical trial learnings**
- **Strengthen the support for pharmacovigilance efforts**
- **Leverage the existing studies to address immediate gaps that would address remaining /emerging research gaps**

Industry Collaboration Opportunities

- Opportunities to scale-up MMD
  - Increased understanding of product preferences:
    - In South Africa, most patients use weekly pill boxes and, therefore, larger bottles for a 6 month supply of drugs are not a concern. However, in other countries, patients have expressed issues around privacy, ease of transport and storage.
  - Increased patient-centric focus to avoid MMD bottlenecks:
    - Lack of access to viral load, or variability in the definition and providers' perception of stability, need to be proactively addressed.
- Continue coordination for the adequate scale-up in manufacturing of optimal pediatric ARVs, and the accelerated development of newer formulations (such as LPVr 4-1, DTG 5 mg, DTG 10 mg)
- Harmonize the product packaging for TLD and drugs in the development pipeline
  - Integrate understanding of patients product preferences early in development
  - Continue work with the community to ensure there is a common recognition of TLD in countries where patients may be confused by different pill colors / packaging

Questions/Opportunities?

THANK YOU!

PEPFAR

U.S. President's Emergency Plan for AIDS Relief

ART Optimization

COP 20 planning / FY 20 Implementation

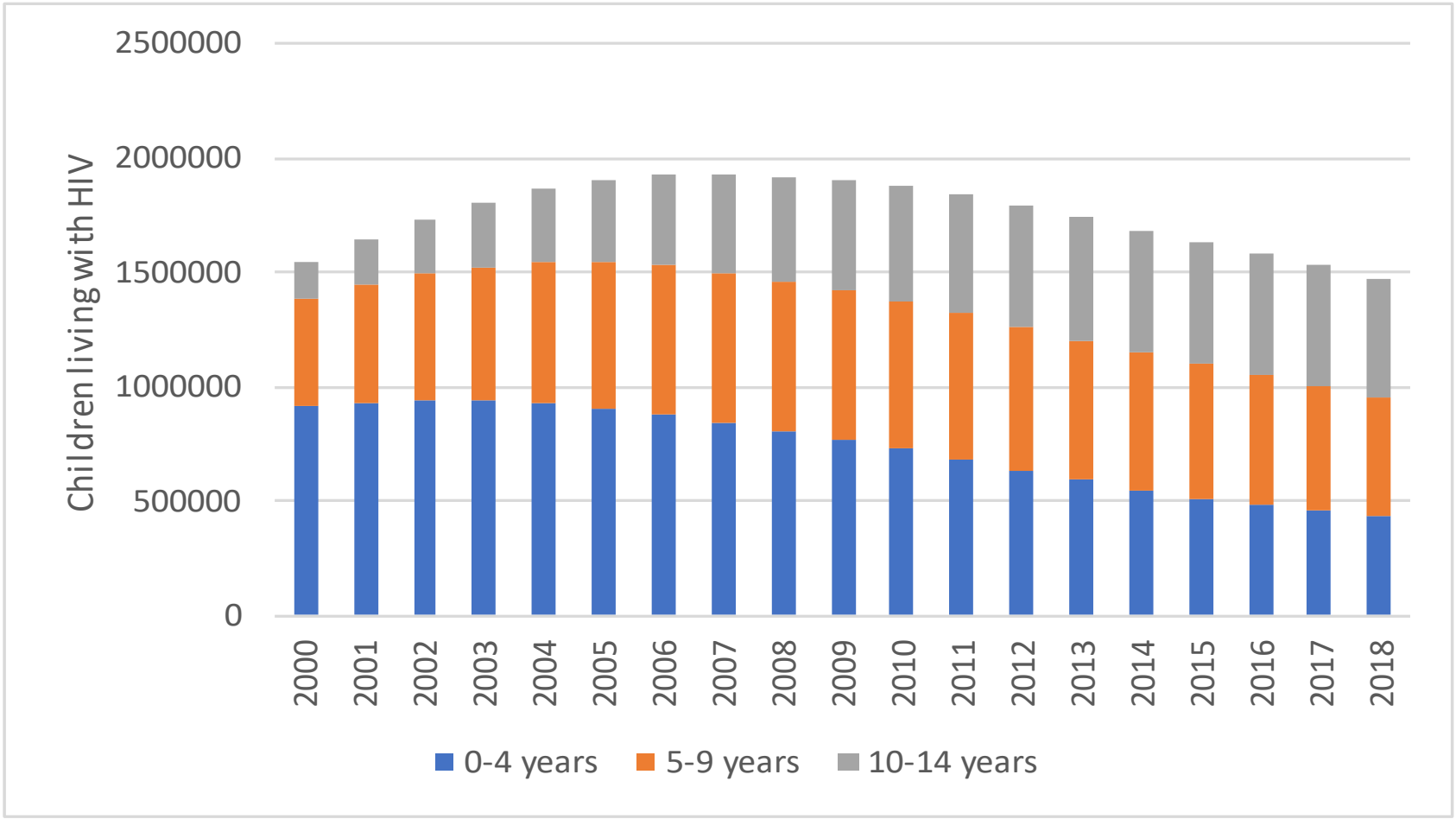
Hilary Wolf| November 26, 2019

FY' 19 Results

- Nearly 15.7 million people on lifesaving antiretroviral treatment
- Nearly 700,000 children on lifesaving antiretroviral treatment

INDICATOR	CUMULATIVE RESULTS
TX_CURR	15,667,099

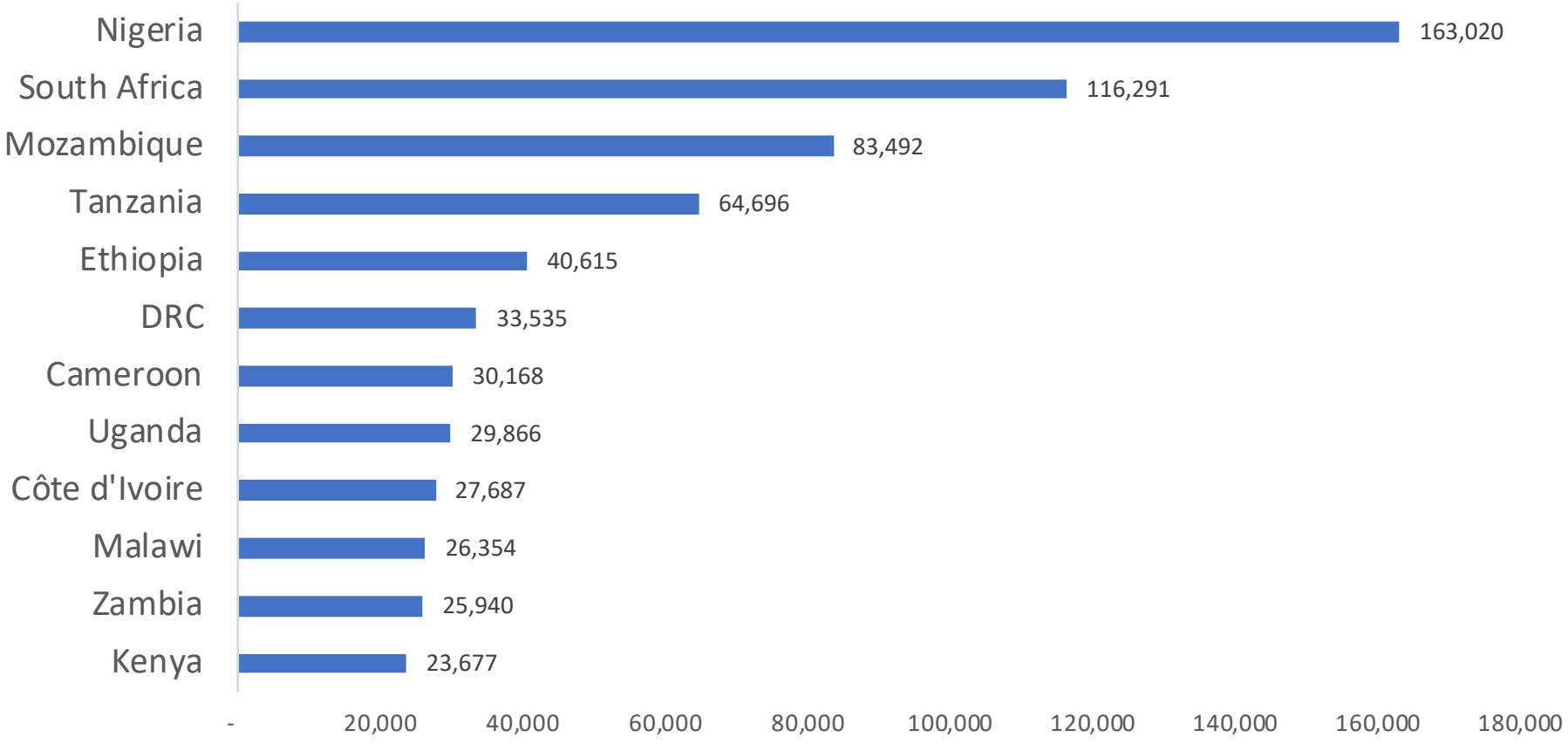
1.5 million Children living with HIV in 2018



CLHIV increasingly school-aged (5-9) and adolescent (10-14) and less likely under 5 years old

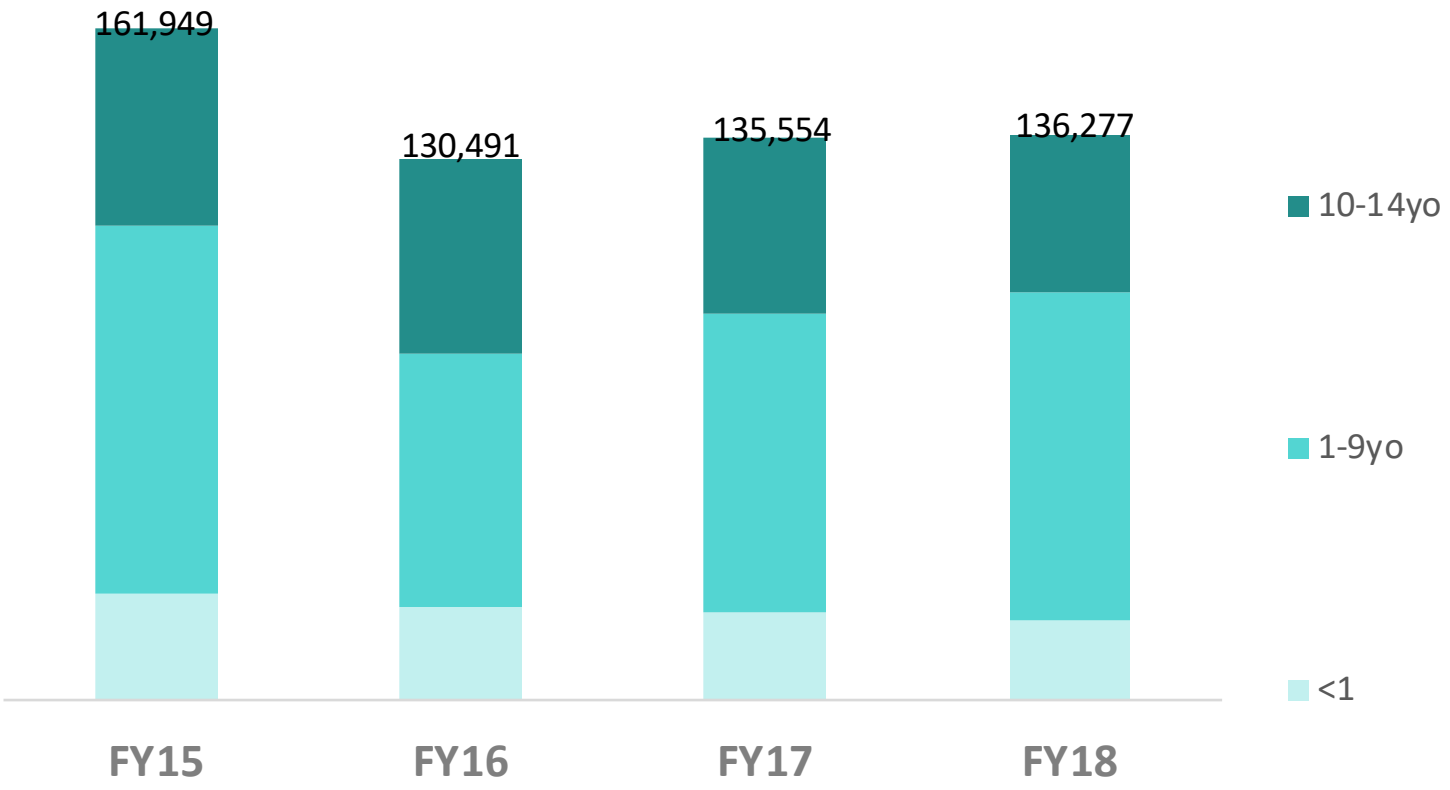
UNAIDS 2019

12 countries account for 80% of the HIV treatment gap, or approximately 700,000 children needing treatment



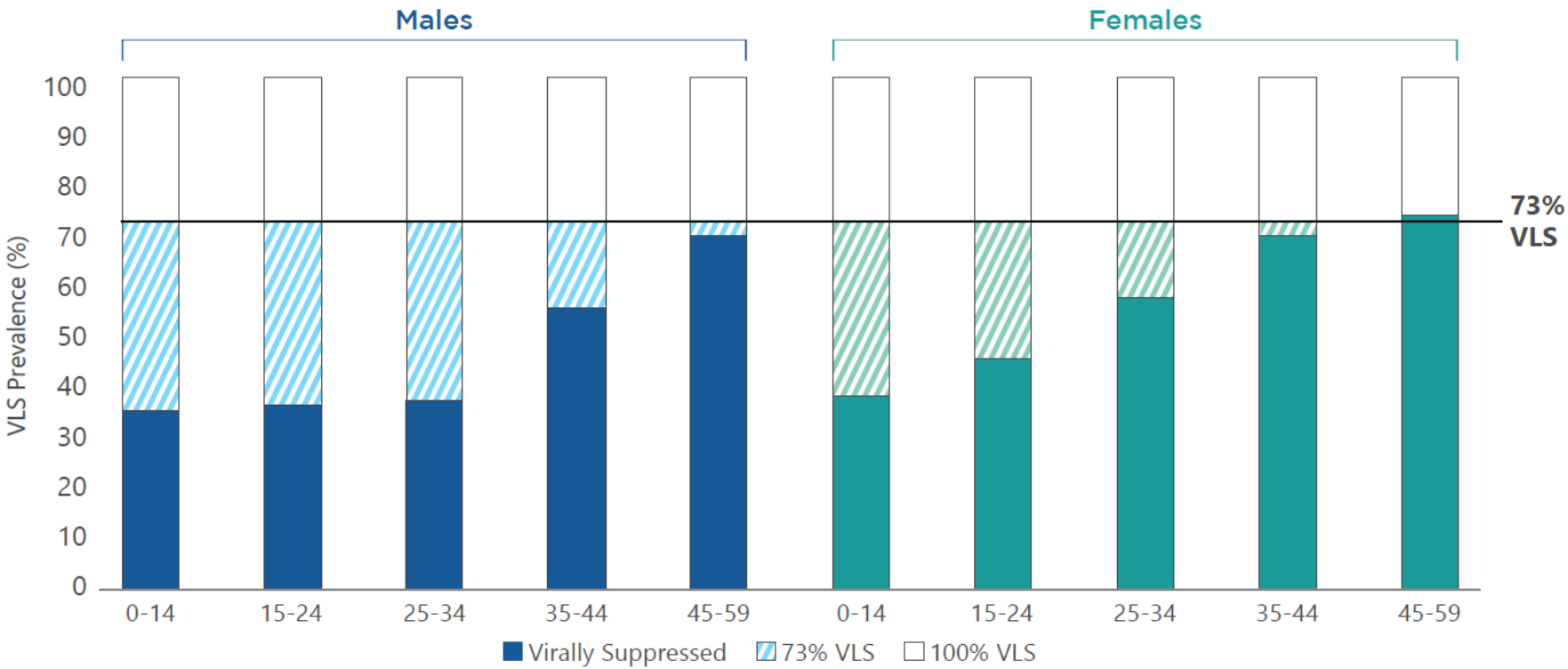
Source: UNAIDS and THEMBISA (SA) CLHIV estimates, 2018; UNAIDS <15 ART coverage, 2018; APR18 TX_CURR <15

We are still finding *children* (<15) living with HIV



Source: Panorama, Age and Sex Disaggregates: All PEPFAR OUs Dashboard; HTS_TST_POS 1-9; (<1) FY15-17 Cum Results PMTCT_EID_POS and FY18 Cum Results PMTCT_HEI_POS

PHIAs also demonstrate large gaps in population level VLS



Source: https://www.pepfar.gov/documents/organization/286448.pdf Lesotho, Malawi, Namibia, Swaziland, Tanzania, Uganda, Zambia, and Zimbabwe.

Draft Minimum PEPFAR Program Requirements COP 2020

1. **Rapid optimization of ART by offering TLD to all PLHIV weighing >30 kg (**including adolescents and women of childbearing potential**),** transition to other **DTG-based regimens for children** weighing ≥20kg, removal of all nevirapine-based regimens
2. Adoption and implementation of differentiated service delivery models**, including six-month multi-month dispensing (MMD**) and delivery models to improve identification and ARV coverage of men and adolescents
3. All eligible PLHIV, including children, should **complete TB preventive treatment (TPT)** by end of COP20, and **cotrimoxazole,** where indicated, must be fully integrated into the HIV clinical care package at no cost to the patient

TLD for PLHIV >30 kg

- **TLD** is the PEPFAR recommended option for both **first and second** line
- We anticipate that **>90% of PLHIV in care will be on TLD**
- Recommend **TLD** for patients who failed TLE in settings where adherence counseling is done well and VL can be assured 3-6 months after the switch
- Need for product and **packaging that is stable over 90 – 180 days** after seal is broken in settings with high heat and humidity

Updates 2019 WHO Guidelines on 1st line ART regimens

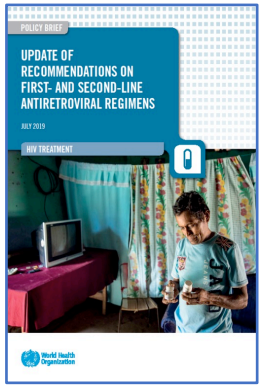
First-line ART regimens[a]

1. Dolutegravir (DTG) in combination with a nucleoside reverse-transcriptase inhibitor (NRTI) backbone is recommended as the preferred first-line regimen for people living with HIV initiating ART
   - Adults and adolescents[b] *(strong recommendation, moderate-certainty evidence)*
   - Infants and children with approved DTG dosing *(conditional recommendation, low-certainty evidence)*
2. Efavirenz at low dose (EFV 400 mg) in combination with an NRTI backbone is recommended as the alternative first-line regimen for adults and adolescents living with HIV initiating ART[c] *(strong recommendation, moderate-certainty evidence)*
3. A raltegravir (RAL)-based regimen may be recommended as the alternative first-line regimen for infants and children for whom approved DTG dosing is not available *(conditional recommendation, low-certainty evidence)*
4. A RAL-based regimen may be recommended as the preferred first-line regimen for neonates *(conditional recommendation, very-low-certainty evidence)*

[a]See Table 1 for ARV drug selection.
[b]See Box 2 on women and adolescent girls of childbearing potential using DTG.
[c]Except in settings with pretreatment HIV drug resistance to EFV/nevirapine (NVP) exceeding 10%.

NEW

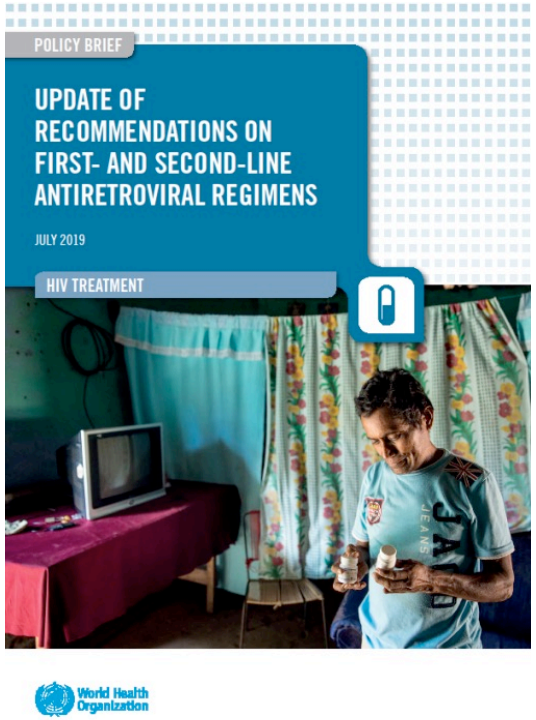
NEW



If LPV/r solid oral dosage formulations are not available

Policy and Guideline: National Updates

- Support MoH to:
  - Prioritize TLD use down to 30 kg for adolescent boys and girls
  - Adopt DTG 50 mg film-coated tab use down to 20 kg in first- and second-line regimens
  - Adopt LPV/r solid formulations for children <20 kg (unable to take film coated DTG)
  - Adopt routine transition to optimized regimens for children already on ART
  - Adopt use of RAL * and DRV/r for infants/children failing/intolerant of LPV/r and not yet big enough for DTG
  - Continue plans to phase out NVP and EFV



*limit use of RAL to kids < 3 years of age failing or intolerant to LPV/r regimens

Overview of PEPFAR-recommended Newer Pediatric ARVs/Formulations

	LPV/r Oral Pellets*	LPV/r Oral Granules*	RAL Granules for Oral Suspension	RAL Chewable Tablets	DRV Tablet (with RTV)
Eligible Pediatric Population	1) Age: 3+ months, and 2) Unable to fully swallow intact LPV/r pediatric tablet	1) Age: 2+ weeks, and 2) Unable to fully swallow intact LPV/r pediatric tablet	Neonates (0 – 28 days of age) only who had a HIV+ birth test; to be used only during the first four weeks of life prior to transition to RAL chewable tablets or LPV/r oral solution.	To only serve as a temporary bridge for the shortest time possible between RAL granules and LPV/r solid formulation	CLHIV (≥3yo) failing a PI-based regimen
PEPFAR Preferred Formulation	40 mg/10 mg capsule	40 mg/10mg sachet	100 mg sachet	25 mg (can be chewed, crushed or dispersed for administration)	DRV 75 mg tablet (with RTV 25** mg or RTV 100 mg tablet – cannot be crushed)

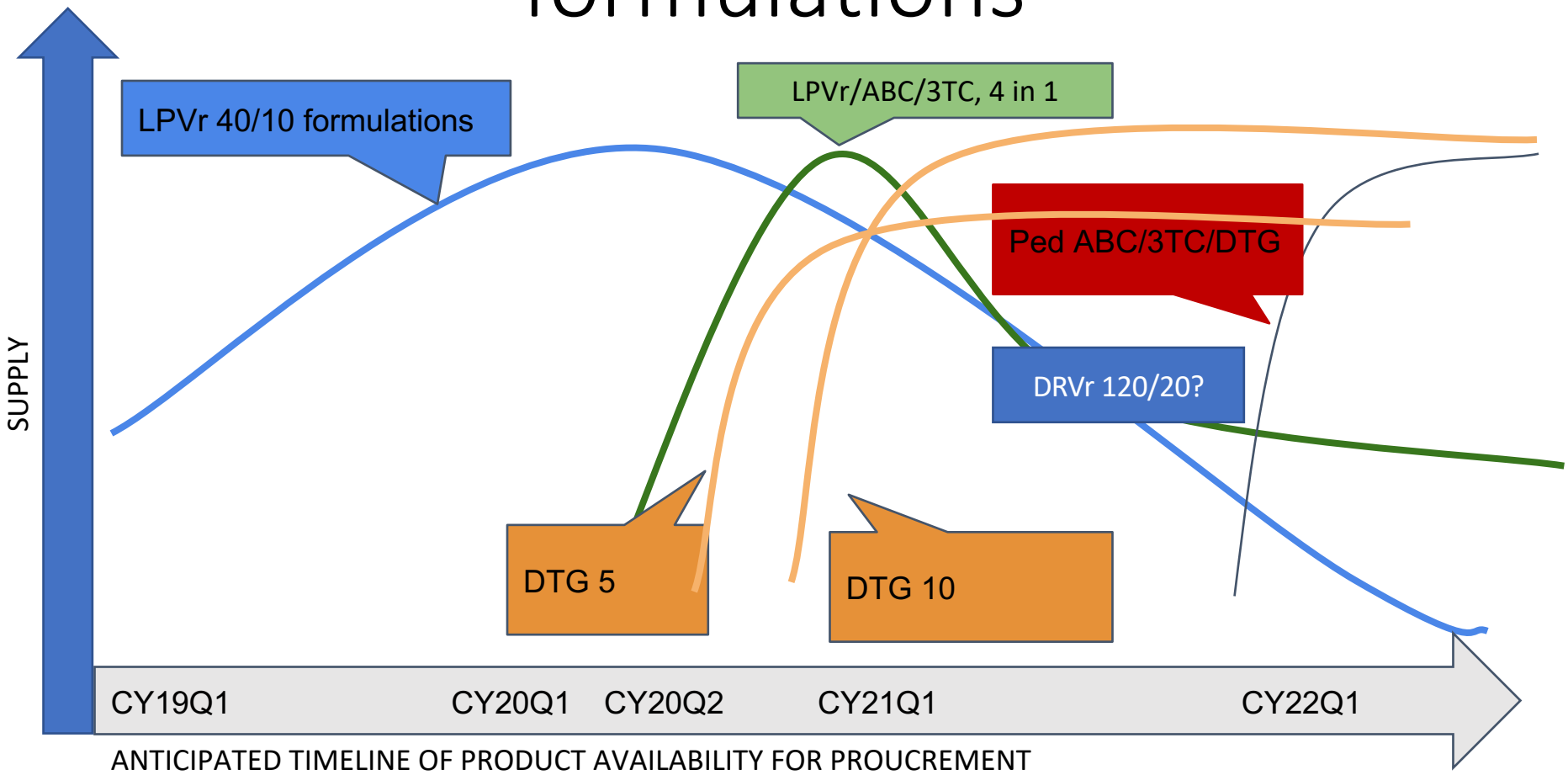
*Countries are discouraged from procuring both LPV/r pellets and granules. Pediatric and supply chain ISMEs are available to support countries to determine whether to procure LPV/r pellets or granules.

**RTV 25 mg can only be procured with funding from Global Fund. PEPFAR funds cannot be used to procure RTV 25 mg but can be used to procure RTV 100 mg.

Vatican Consortium: Strengthened Commitments to Accelerating Priority Pediatric ARV Development & Uptake and Diagnostics

Leaders of major pharmaceutical and medical technology companies, multilateral organizations, donors, governments, organizations providing or supporting services for children living with HIV, and other key stakeholders participated in a High-Level Discussion on Scaling Up Early Diagnosis and Treatment of Children and Adolescents.

Product life cycle of new pediatric formulations



CLHIV Who Could Benefit from Taking pDTG

- As of Q4, 2019 we had **346,300 CHLIV** (age 0-9) on treatment in PEPFAR programs
- Predict the majority of these CHLIV who are < 20 kg would be switched to DTG when pediatric formulations become available (contingent on FDA approval)
- This number will increase as we find more undiagnosed children
- CHAI estimates ~**500-600K CLHIV eligible for pDTG** (i.e. <20kg) in 26 highest volume countries
- Children who can't tolerate DTG or are ineligible based on weight should be switched to **LPVr/ABC/3TC, 4 in 1 products** (contingent on FDA approval)

Draft COP20 Guidance on MMD

- DSD models provide a critical solution to retention and adherence barriers
- Stable ART patients at should be offered **six months of ART** with refills and adoption of fast track refill models
- Children, adolescents, pregnant and breastfeeding women, key populations and foreign nationals who meet criteria for being stable on ART should all have access to MMD

Draft COP20 Guidance on MMD

Children 2-5 years

- 3 monthly refills (including co-trimoxazole refill, disclosure process check-in) and clinical visits *(one visit for refills and clinical consultations)*
- Suppressed and on the same regimen for 3 months without serious intercurrent illness

Children 5-10 years

- 3 monthly ART refills-delinked from clinical consultation visits, can be managed by lay providers
- 6-monthly clinical visits with family friendly scheduling Nurses can carry out clinical consultations and reissue prescriptions

Adolescents

- Similar clinical criteria used for adults in determining eligibility for MMD with consideration for psychosocial support outside of the clinical setting

Draft COP20 Guidance on MMD

- 75-80% of all individuals should be stable on treatment and be receiving MMD – of this ~ half should be on a minimum of 3 months and other half should have 6 month refills
- **No 30 ARV size bottles will be purchased after Jan 1, 2020**. All clients should be given a minimum of 3 months' worth of drug supply even if a follow-up visit is needed in less than 3 months
- National formulary documents in-country should be revised to include **larger pack sizes**
- Identify safe storage requirements for larger pack sizes
- Stable patients transitioning to TLD should still be considered stable patients and eligible for MMD

PEPFAR

U.S. President's Emergency Plan for AIDS Relief

Thank You!

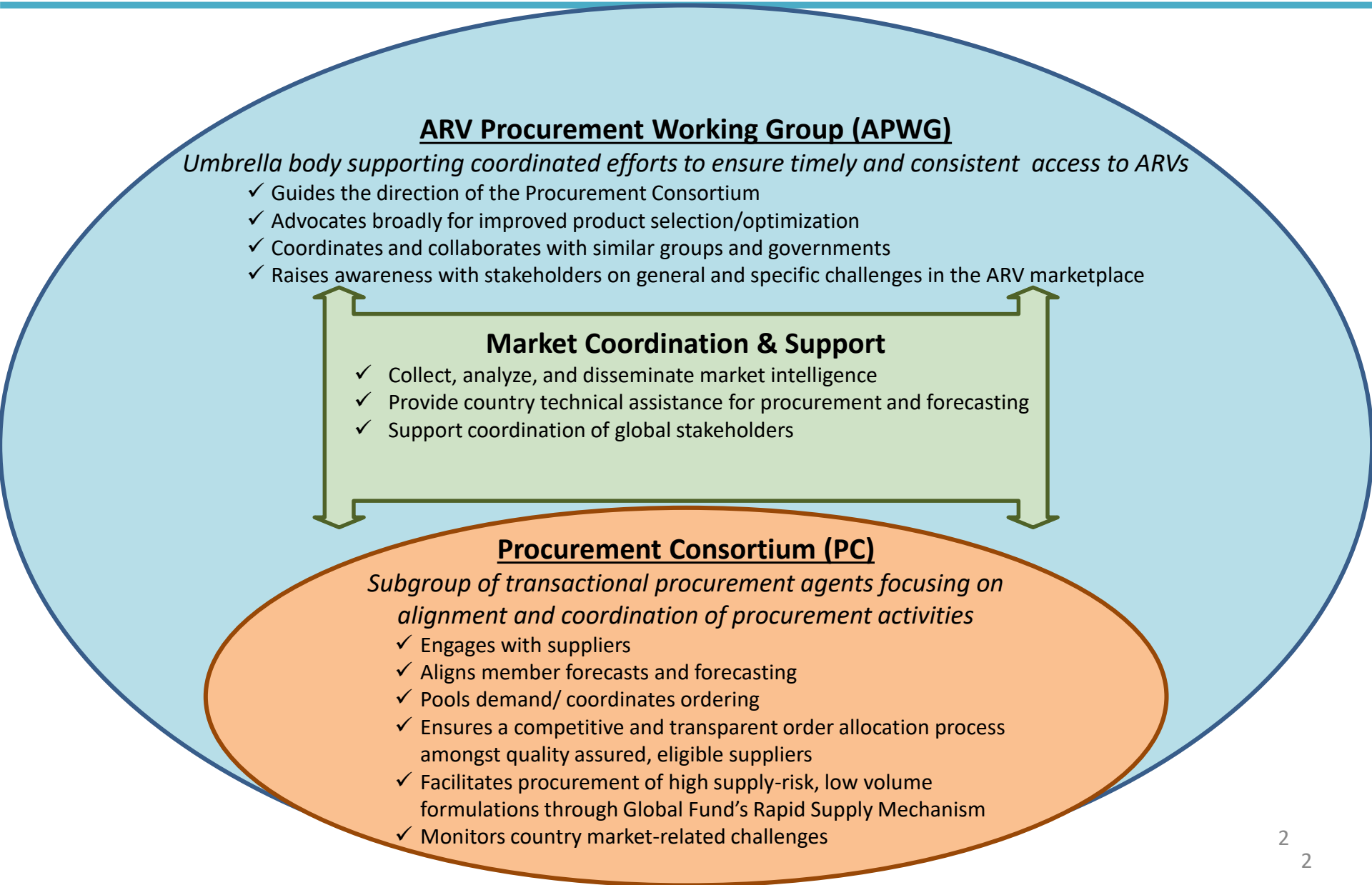
16 YEARS OF SAVING LIVES THROUGH AMERICAN GENEROSITY AND PARTNERSHIPS

ARV Buyer Seller Summit

APWG support on treatment optimization

November 26th, 2019

WORKING GROUP STRUCTURE



APWG role in Optimal Formulary List

- Advice on products to be included in the Optimal and Limited Use list
- Highlight procurement and supply elements for each product
- Initiate conversations with suppliers on production capacity and supply timelines
- Identify products for monitoring via quarterly APWG calls

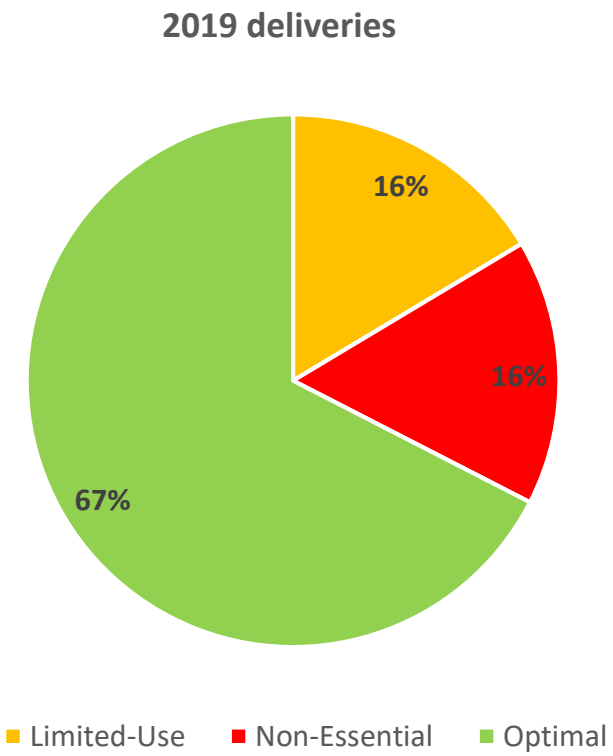
POLICY BRIEF

THE 2018 OPTIMAL FORMULARY AND LIMITED-USE LIST FOR PAEDIATRIC ARVS

APWG role in advocating ordering Optimal formularies

- APWG buying organizations only show products on their catalogue that support treatment optimization
- Dialogue with countries to transition towards optimal formularies
- Highlight supply chain and procurement advantages of treatment optimization to countries
- Organize webinars on supply chain related elements of treatment optimization
- Publish recommendation letters for transition to optimal formularies

Orders placed by APWG members mostly for Optimal formulations and formulations recently moved



Optimal Formulations	Quantity	%
ABC/3TC (120/60 mg) Tablet (Disp) - 30	4,200,000	41%
LPV/r (100/25 mg) Tablet (HS) - 60	1,700,000	16%
ABC/3TC (120/60 mg) Tablet (Disp) - 60	1,300,000	13%
NVP (50 mg/5 ml) Oral Solution - 100ml	895,000	9%
AZT/3TC (60/30 mg) Tablet (Disp) - 60	890,000	9%
LPV/r (40/10 mg) Oral Pellet - HS - 120	640,000	6%
LPV/r (40/10 mg) Oral Granule - HS - 120	240,000	2%

Limited-Use Formulations	Quantity	%
AZT/3TC/NVP (60/30/50 mg) Tablet (Disp) - 60	1,700,000	68%
EFV (200 mg) Tablet (Scored) - 90	675,000	27%
LPV/r (80 mg + 20 mg/ml) Oral Solution	55,000	2%

Non-Essential Formulations	Quantity	%
ABC/3TC (60/30 mg) Tablet (Disp) - 60	1,700,000	73%
AZT (50 mg/5 ml) Oral Solution - 240ml	400,000	16%
NVP (50 mg/5 ml) Oral Solution - 240ml	135,000	6%

Quantities are based on orders placed for delivery in 2019 as per Q3 APWG data

Demand and supply traffic light to support scale-up of optimal formularies

In-country delivery quarter[1]	Lopinavir/Ritonavir 40mg/10mg, Pellets, 120 capsules	Lopinavir/Ritonavir 40mg/10mg, Oral Granules, 120 sachets	Lopinavir/Ritonavir 100mg/25mg, Tablets
Q1 2020			
Q2 2020			
Q3 2020			
Q4 2020			
Q1 2021			
Q2 2021			

- Dashboard on supply availability, production and lead times
- Facilitates messaging to countries on order times and scale-up possibilities
- Active monitoring between suppliers and countries

The APWG website includes relevant optimization documents

https://www.arvprocurementworkinggroup.org/home

The APWG now has a dedicated website to host all important documents and communications!

Check back often as new documents are released.

The website includes:

- The quarterly demand forecast
- Bi-annual newsletters
- Recorded webinars
- Key recommendations and product guidance documents
- A LPV/r product dashboard

7

APWG Anticipated Demand Forecast published quarterly

APWG Quarterly Anticipated Demand Forecast

- Provides summary of **expected orders over 12-18 months** that are visible to APWG members
- Includes **pediatrics ARVs, low-volume adult ARVs, and adult products in transition**
- Shared **quarterly** (usually third month of each quarter)
- Includes **summary of countries that have already placed or are expected to place orders** for priority products
- Provides a **breakout of procurement agents sourcing orders for each member country**

APWG Anticipated Demand Forecast as of June 19, 2019: *By Expected Delivery Quarter*

(total pack volumes across all procurement agents by expected delivery quarter, defined as the quarter in which ARVs are expected to be handed over to the local client according to the respective incoterms)

Target Delivery Quarters →	Q3 2019	Q4 2019	Q1 2020	Q2 2020	Q3 2020	Q4 2020	TBD
Optimal Pediatric Products							
ABC/3TC (120/60 mg) Tablet (Disp) - 30	1,147,912	1,125,921	269,091	24,271	25,412	26,054	181,137
ABC/3TC (120/60 mg) Tablet (Disp) - 60	152,644	200,060	255,785	-	-	-	6,010
AZT (50 mg/5 ml) Oral Solution - 100ml	35,516	21,795	-	23,740	-	-	-
AZT/3TC (60/30 mg) Tablet (Disp) - 60	144,993	49,420	46,012	73,072	29,810	31,973	90,571
LPV/r (100/25 mg) Tablet (HS) - 60	440,553	381,299	117,296	143,839	69,461	73,747	20,008
LPV/r (100/25 mg) Tablet (HS) - 120	84,604	-	73,130	-	-	-	-
LPV/r (40/10 mg) Oral Pellet - HS - 120	132,031	97,801	176,580	176,813	127,845	145,640	78,255
LPV/r (40/10 mg) Oral Granule - HS - 120	46,173	85,386	20,000	215,560	33,111	-	-
NVP (50 mg) Tablet (Disp) - 30	109,564	6,360	7,953	6,707	6,350	6,242	12,243
NVP (50 mg) Tablet (Disp) - 60	35,704	62,058	40,000	13,378	21,840	-	9,417
NVP (50 mg/5 ml) Oral Solution - 100ml	281,059	160,546	204,762	47,172	4,932	4,932	122,309
RAL (25 mg) Tablet (Scored) - 60	5,455	-	-	-	-	-	1,000
Limited-Use Pediatric Products							
3TC (50 mg/5 ml) Oral Solution - 100ml	-	-	-	-	-	-	5,208
3TC (50 mg/5 ml) Oral Solution - 240ml	9,270	8,788	7,678	-	-	-	7,872
ABC (60 mg) Tablet (Disp) - 60	1,630	672	-	-	-	-	-
ATV (200 mg) Capsule - 60	-	1,441	1,396	1,387	-	-	-
AZT/3TC/NVP (60/30/50 mg) Tablet (Disp) - 60	504,160	46,432	113,747	296,489	45,261	36,053	122,129
DRV (75 mg) Tablet - 480	-	-	-	-	-	-	-
EFV (200 mg) Tablet (Scored) - 90	387,561	13,548	228,150	11,820	2,960	3,000	68,603
LPV/r (80 mg + 20 mg/ml) Oral Solution - 160ml	2,607	-	-	-	-	-	-
LPV/r (80 mg + 20 mg/ml) Oral Solution - 5x60n	6,130	54,940	39,428	10,767	6,150	6,358	68,166
RAL (100 mg) Granules - 60	-	-	-	-	-	-	1,920
RTV (100 mg) Powder - 30	-	-	-	-	-	-	-
RTV (25 mg) Tablet - 60	-	-	1,350	1,400	1,520	1,710	-
Non-Essential Pediatric Products (top 5 products by volume)							
ABC/3TC (60/30 mg) Tablet (Disp) - 60	203,535	513,367	397,172	697,923	428,141	449,067	249,671
ABC/3TC (60/30 mg) Tablet - 60	28,266	218,639	28,284	115,460	-	-	-
EFV (200 mg) Capsule - 90	168,408	108,825	68,419	16,591	-	-	-
AZT (50 mg/5 ml) Oral Solution - 240ml	42,762	106,930	33,476	40,542	30,750	30,850	10,830
NVP (50 mg/5 ml) Oral Solution - 240ml	7,185	-	67,098	64,880	70,144	69,272	5,385
Adult Products in Transition or Low Volume							
3TC (150 mg) Tablet - 60	123,117	184,030	131,376	57,104	55	85	11,974

Latest quarterly demand forecast and other APWG documents can be found here:
https://www.arvprocurementworkinggroup.org/arv-procurement-working-group-documents

Questions


PEPFAR
The Global Fund
Pan American Health Organization
USAID
FROM THE AMERICAN PEOPLE
i+ solutions
universal access to essential medicines
ICAP
Columbia University Mailman School of Public Health
CLINTON HEALTH ACCESS INITIATIVE
KEMSA
ECS
Unitaid
EPSA
CDC
Centers for Disease Control and Prevention
EXPERTISE FRANCE
unicef
DNDi
Drugs for Neglected Diseases initiative
Elizabeth Glaser Pediatric AIDS Foundation
Réseau
eva
Enfants et VIH en Afrique
IAS
medicines patent pool
MEDECINS SANS FRONTIERES
UNDP
World Health Organization

18-Month Consolidated Forecast

November 2019
Washington, DC

The Global Fund

Republic of South Africa

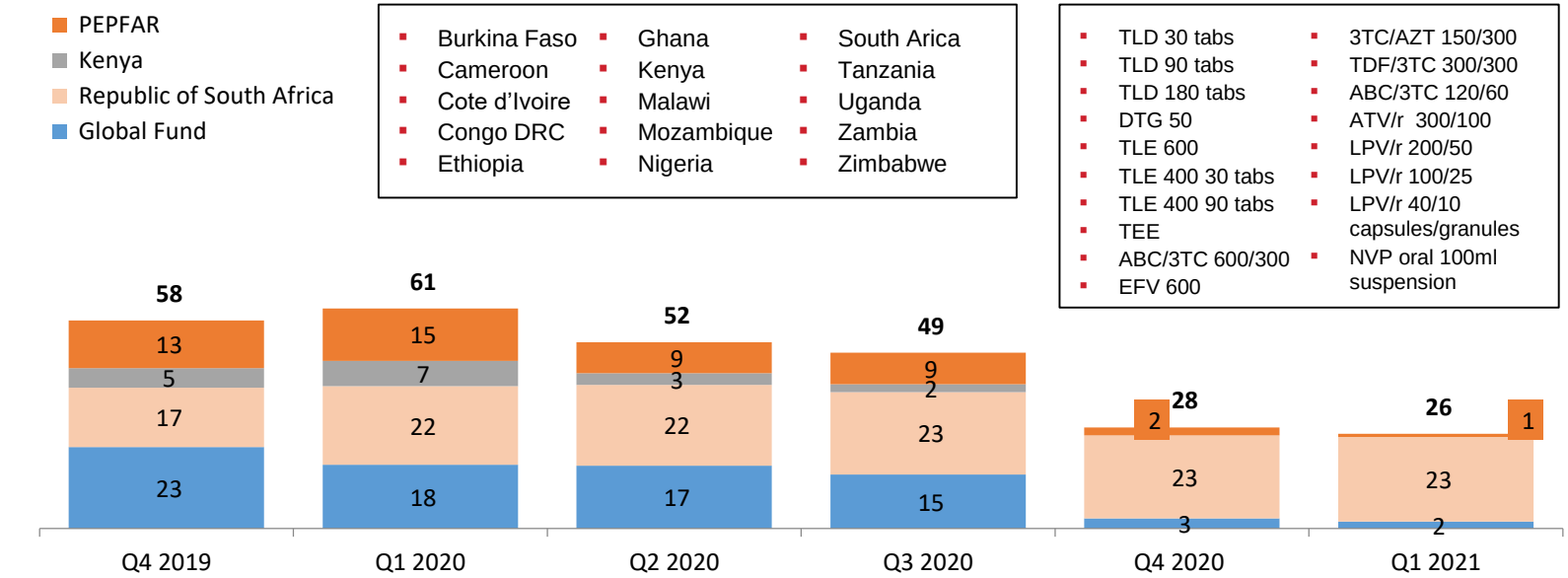
Caveats and limitations to the current version of the visibility data

- **Conservative estimates** based on currently confirmed orders and firm demand
- Prepared based on **data currently available** to The Global Fund, Kenya, PEPFAR, and South Africa
- **Preliminary estimates for the discussion –** and not final purchase commitments
- **May not yet fully capture lead times** between order placement at manufacturer and in-country delivery
- **Eight joint consolidated procurement** forecast

Consolidated Total ARV Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions

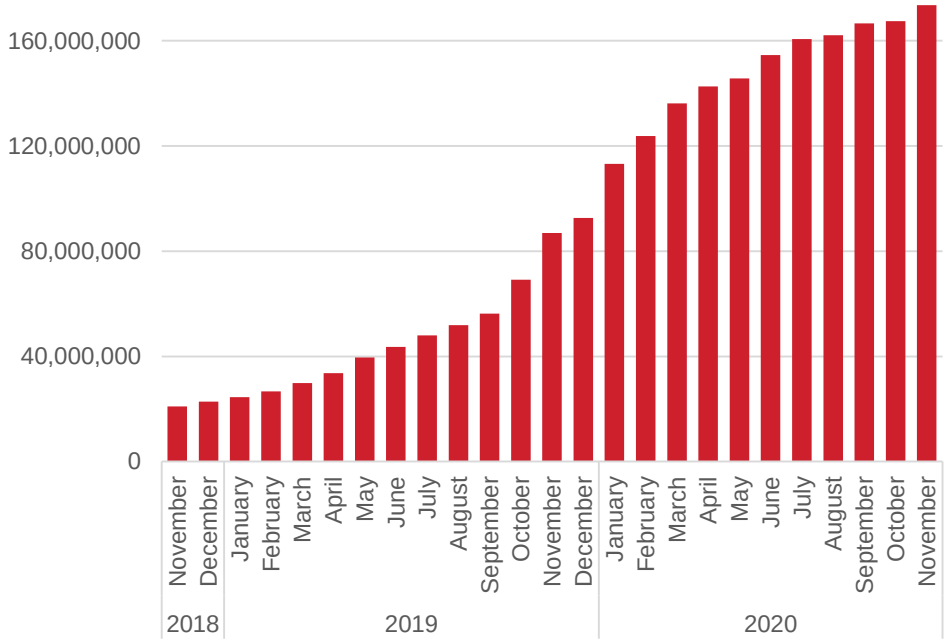


DISCLAIMER: This is an initial version of the forecast, and may contain inaccuracies – please refer to caveats and data limitations on slide 1.
These slides contain a conservative estimate for demand management between the three programs. As such, there may be future volumes not yet financially committed or confirmed.

SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLD Supply Evolution

Cumulative Demand (packs of 30*) Nov 2018 – Nov 2020



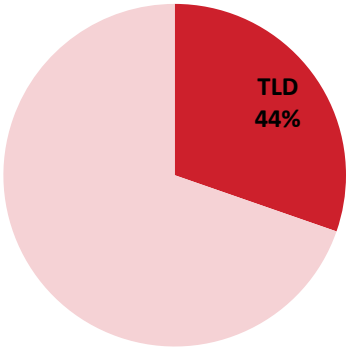
Countries Procuring TLD		
Armenia	Haiti	Papua New Guinea
Benin	Kenya	Peru
Botswana	Laos	Rwanda
Burkina Faso	Lesotho	Senegal
Burundi	Liberia	Sierra Leone
Cameroon	Madagascar	South Africa
Cape Verde	Malawi	Tanzania
Central African Republic	Mali	Timor-Leste
Chad	Mauritania	Togo
Congo Brazzaville	Mongolia	Uganda
Congo DRC	Mozambique	Vietnam
Côte d'Ivoire	Namibia	Yemen
Eswatini	Niger	Zambia
Ethiopia	Nigeria	Zimbabwe
Ghana	Pakistan	
Guatemala	Panama	

Dates refers to in-country delivery date and contains both actual and planned orders; not based on full reporting from all countries.
*Packs of 90 are converted to packs of 30 for consistency purposes.

SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLD Demand as % of Adult First Line

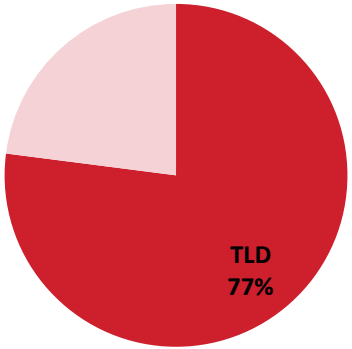
Q4, 2018 - Q1, 2020



November 2018
4th Annual Buyers/Sellers Summit

3x Increase in TLD Volume

Q4, 2019 - Q1, 2021



November 2019
5th Annual Buyers/Sellers Summit

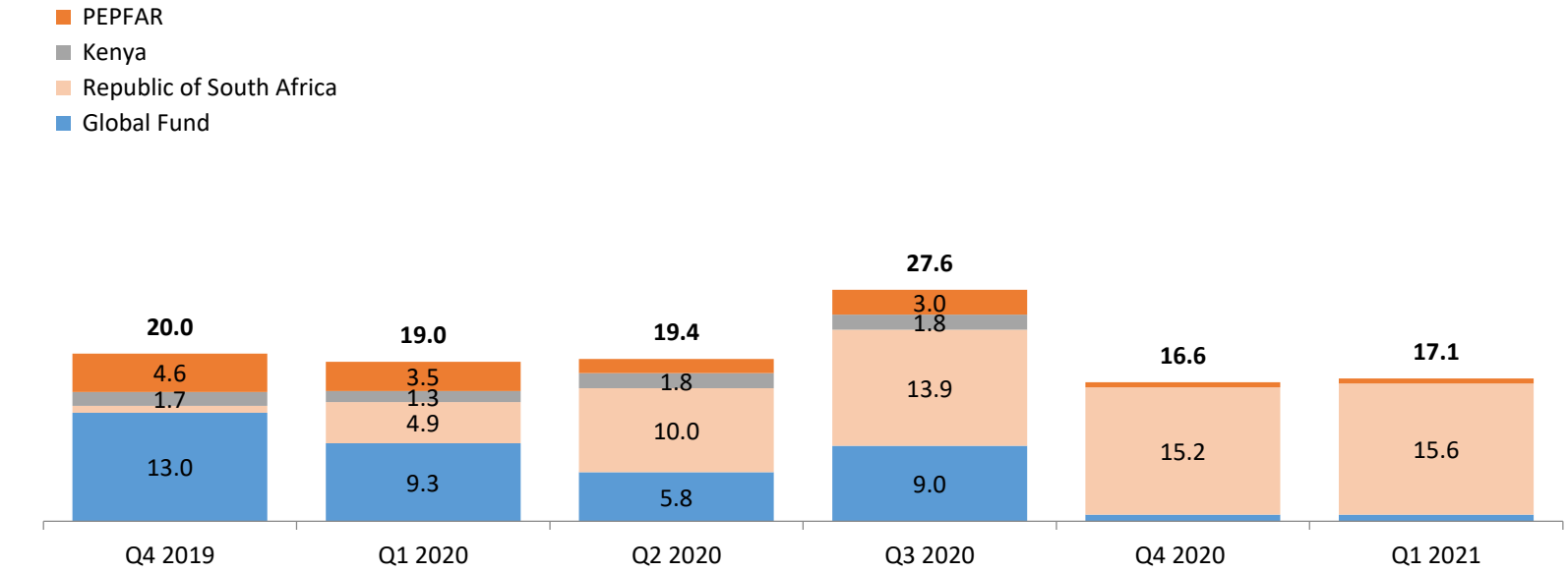
Multi-month packs of TLD (90, 180) and TLE (90) are converted to packs of 30 for consistency (i.e. multiplied by 3 for 90; by 6 for 180)

SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLD 30 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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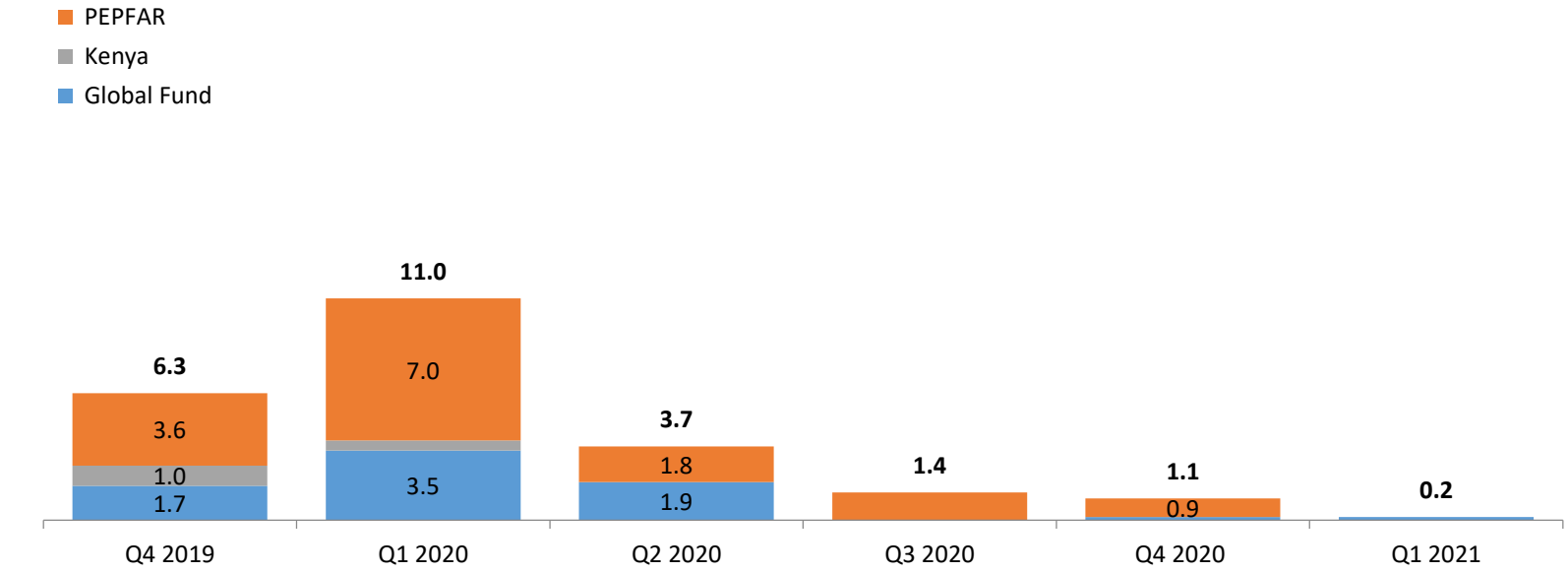
These slides contain a conservative estimate for demand management between the three programs. As such, there may be future volumes not yet financially committed or confirmed.

SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLD 90 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



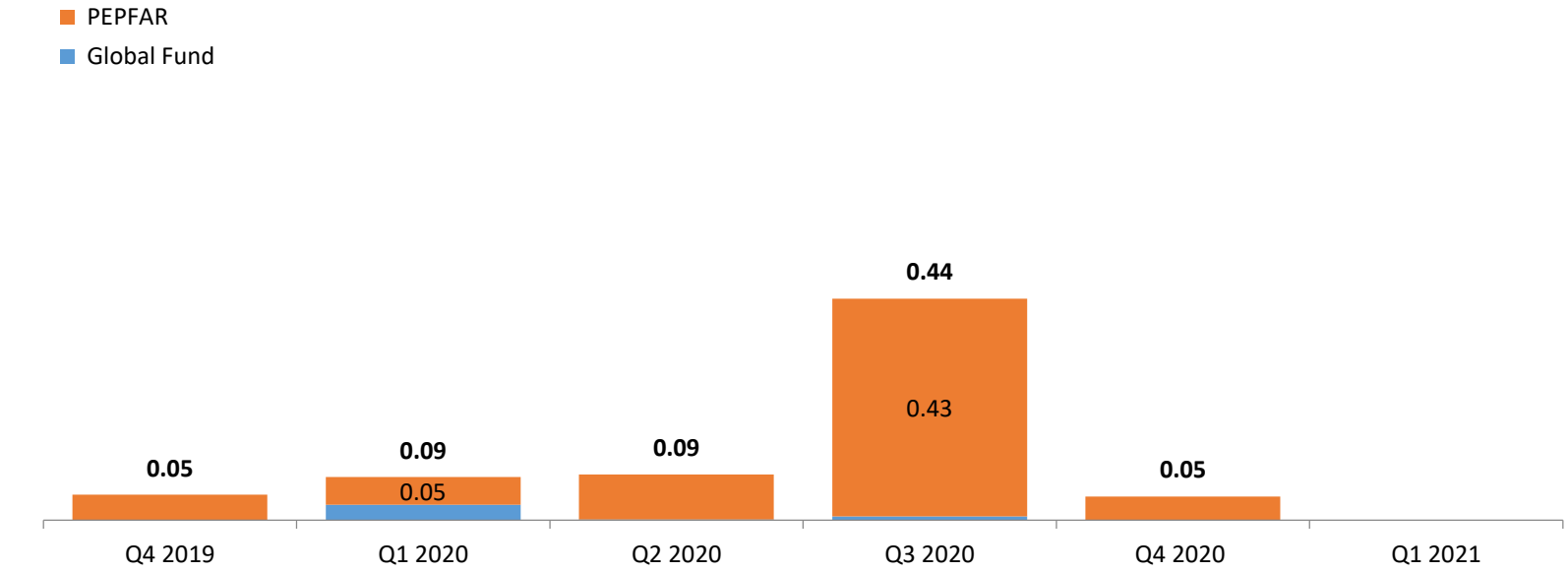
DISCLAIMER: This is an initial version of the forecast, and may contain inaccuracies – please refer to caveats and data limitations on slide 1.
These slides contain a conservative estimate for demand management between the three programs. As such, there may be future volumes not yet financially committed or confirmed.

SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLD 180 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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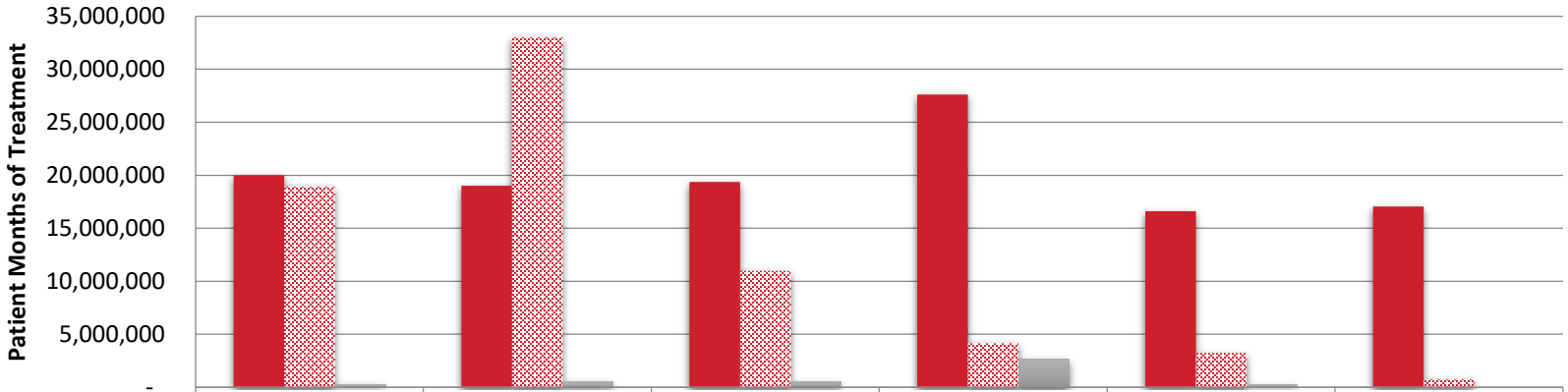
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

Comparison of TLD Pack Size by Patient Months



	2019, Q4	2020, Q1	2020, Q2	2020, Q3	2020, Q4	2021, Q1
TLD 30 tabs	20,001,113	19,009,639	19,381,103	27,609,770	16,596,656	17,056,402
TLD 90 tabs	18,922,909	33,001,683	10,976,848	4,149,489	3,223,566	755,337
TLD 180 tabs	303,180	514,217	545,643	2,637,669	283,992	-

Total Volume of TLD Pack Size Demand Q4 2019 - Q1 2021

- TLD 30 Tabs =119,654,683
- TLD 90 Tabs = 71,029,832
- TLD 180 Tabs = 4,284,701

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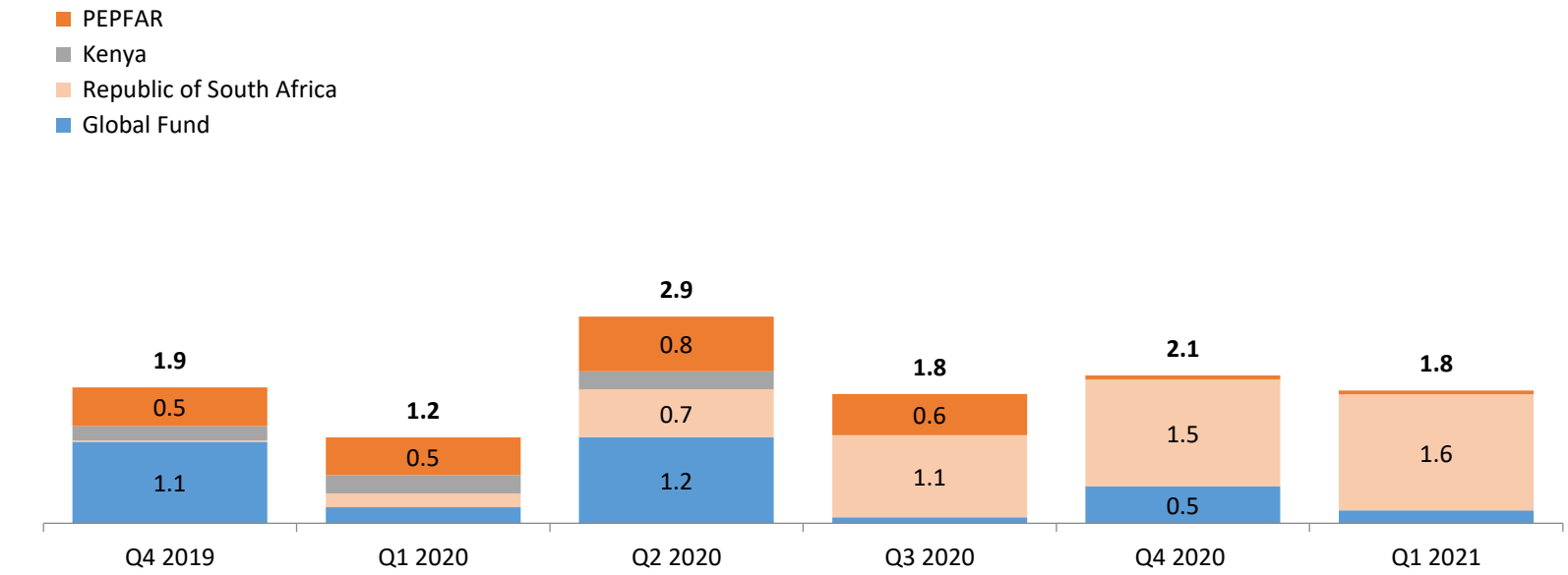
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

DTG 50 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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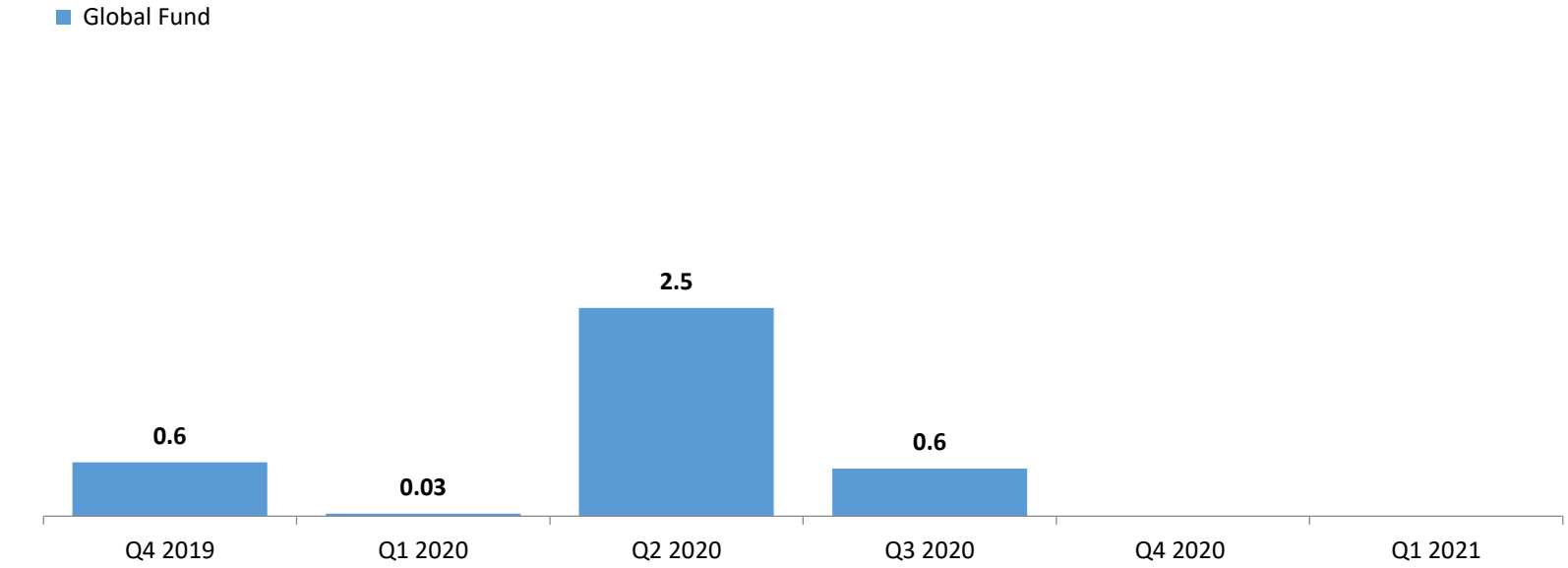
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLE 600 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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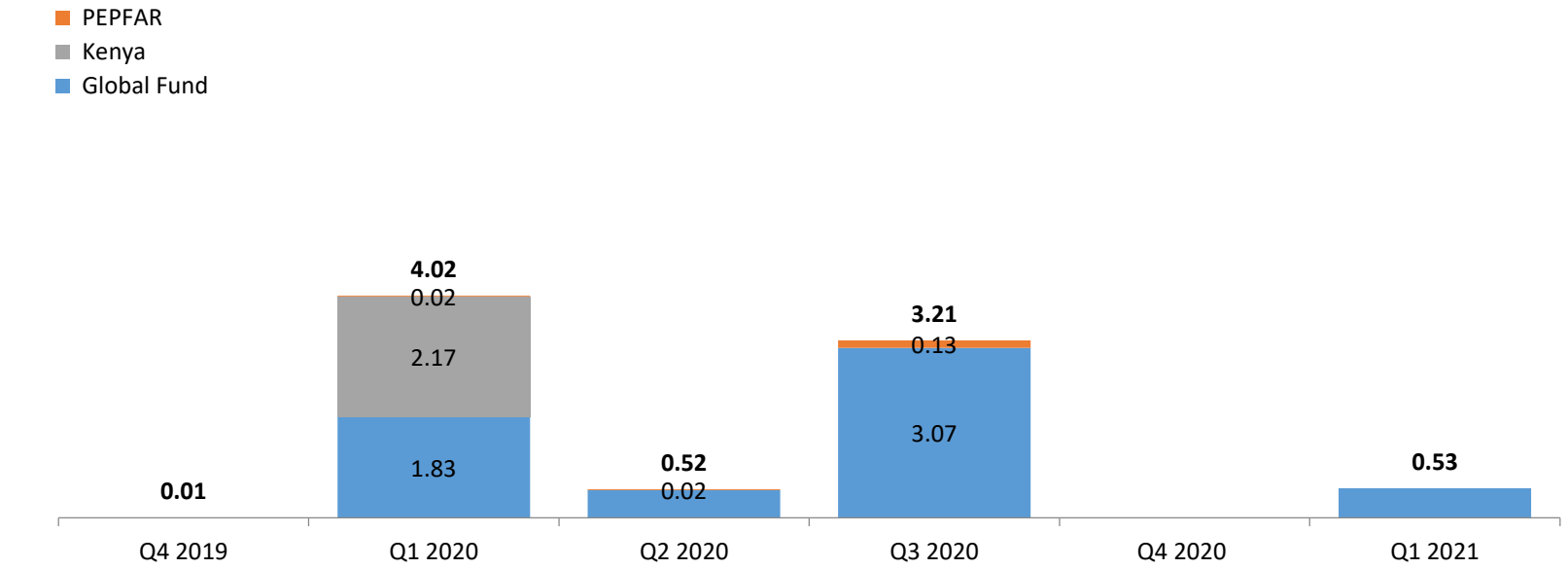
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLE 400 30 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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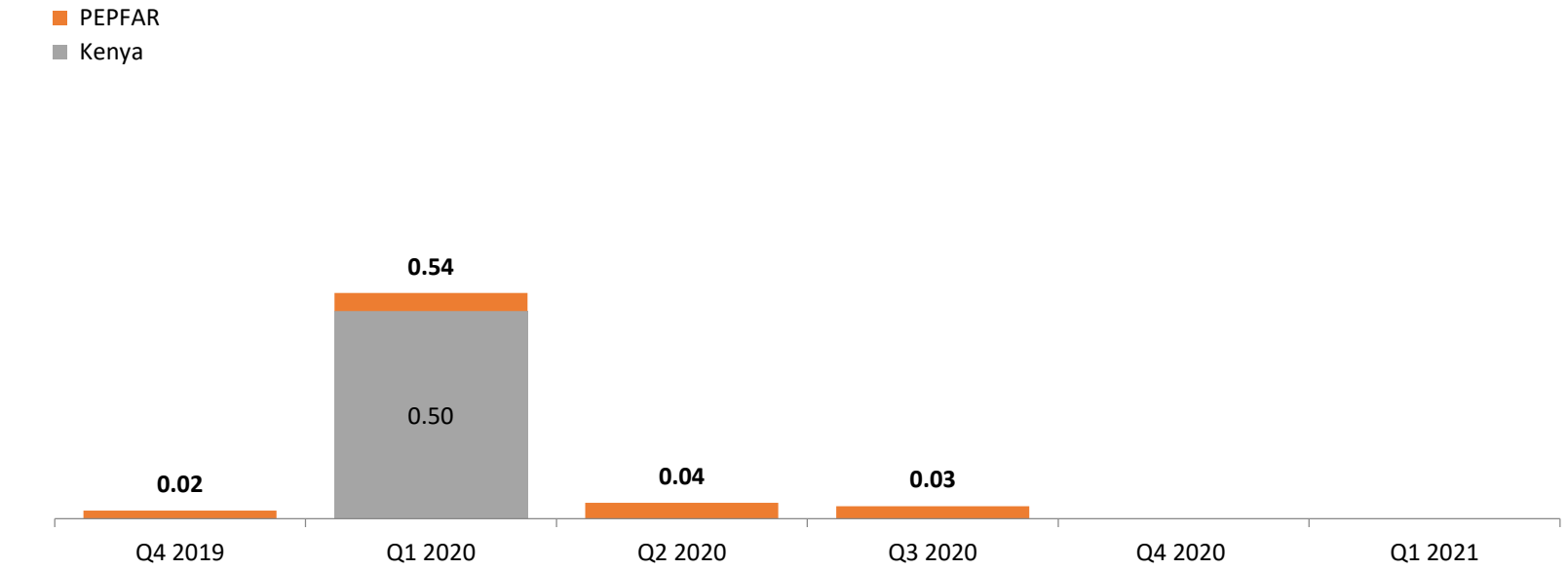
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TLE 400 90 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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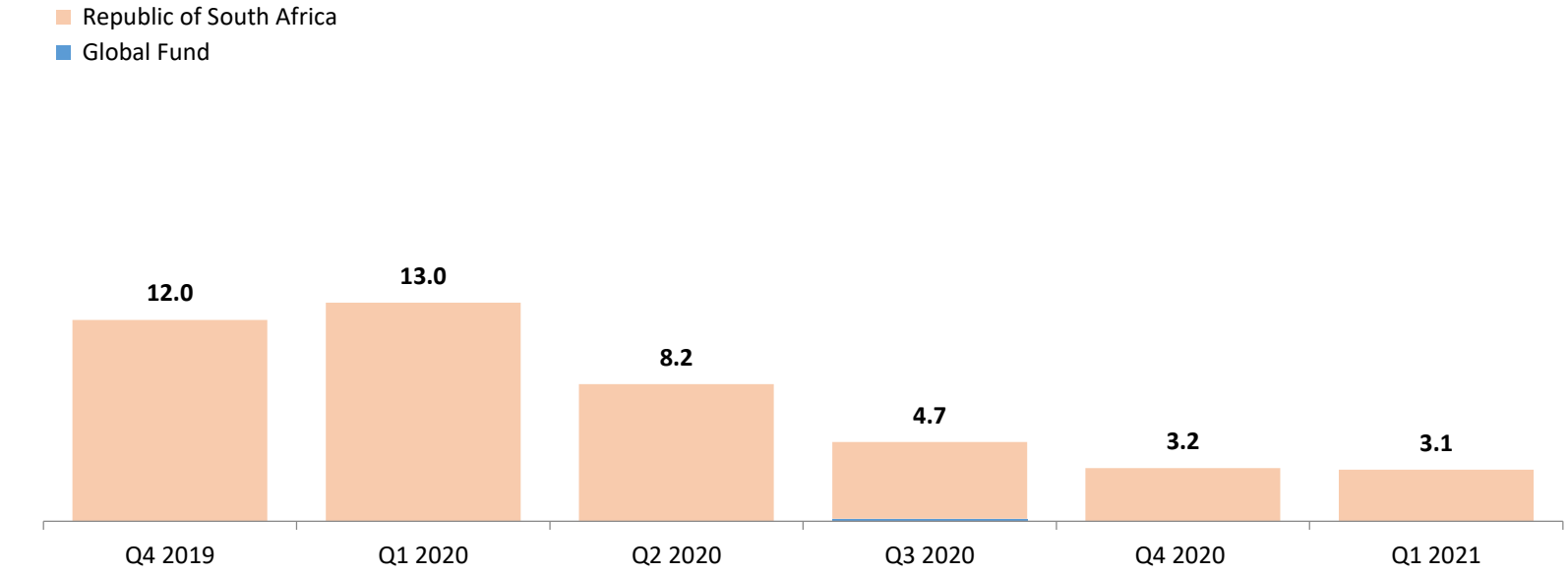
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TEE – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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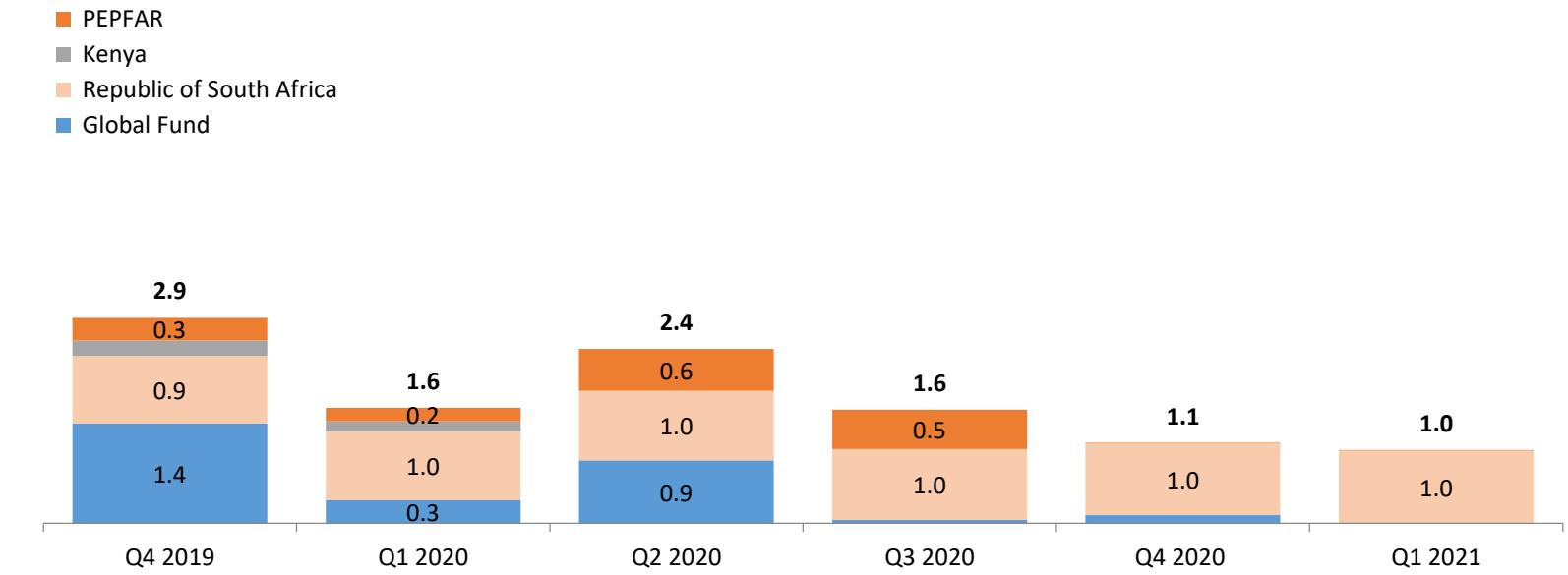
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

ABC/3TC 600/300 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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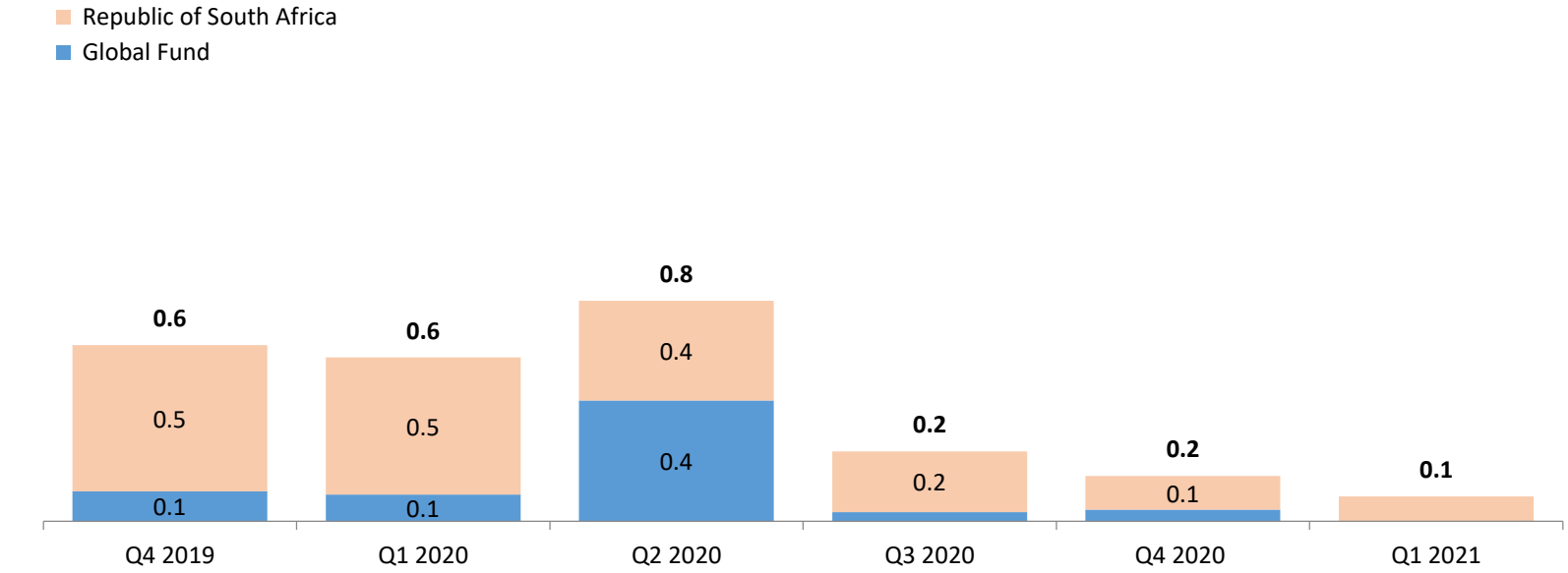
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

EFV 600 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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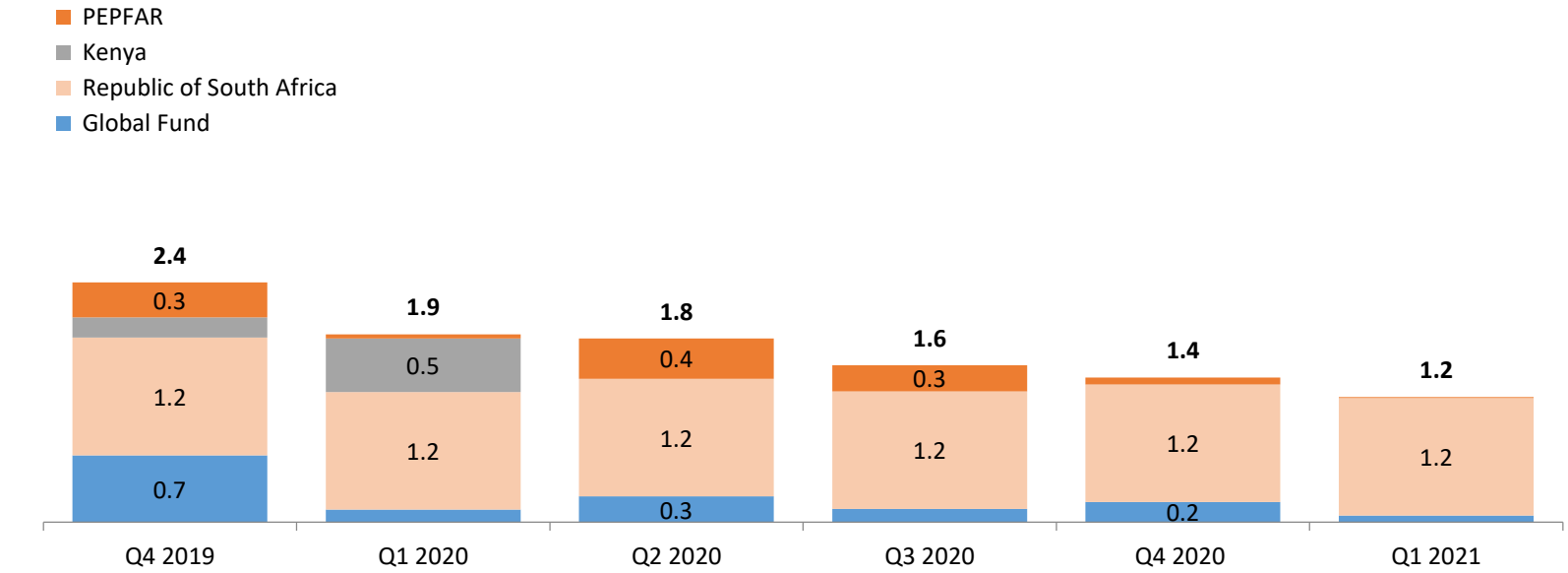
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

3TC/AZT 150/300 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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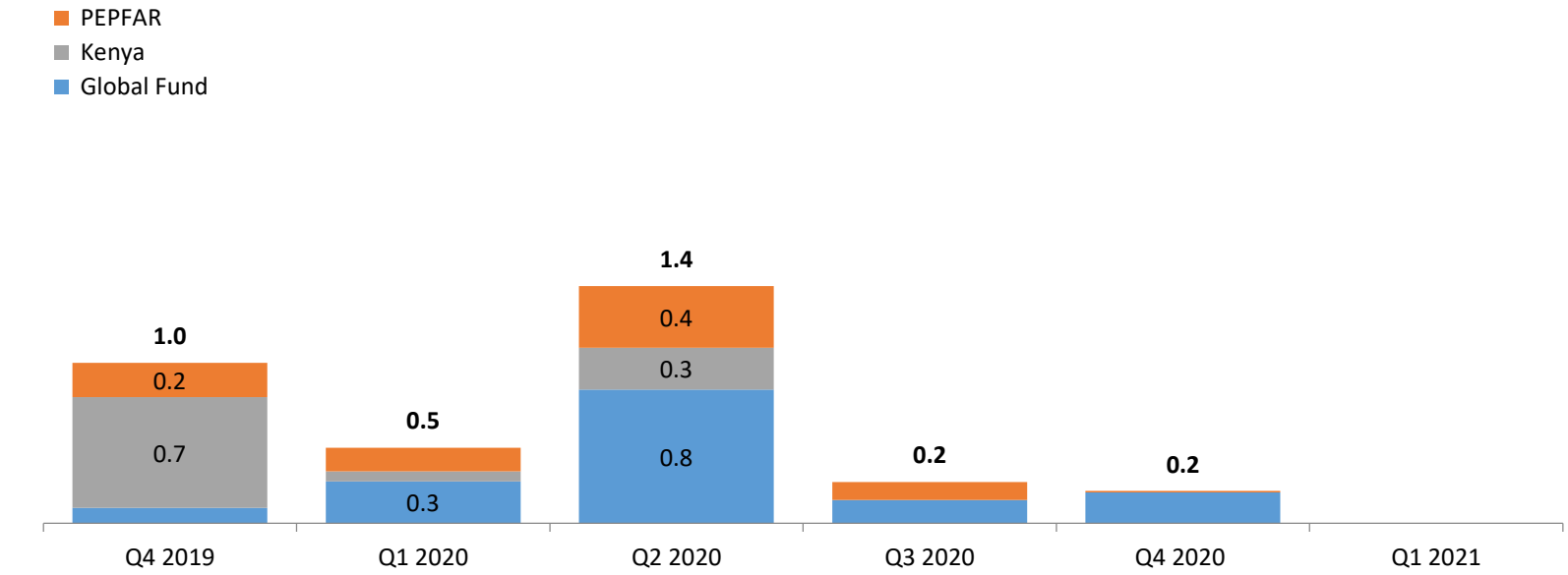
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

TDF/3TC 300/300 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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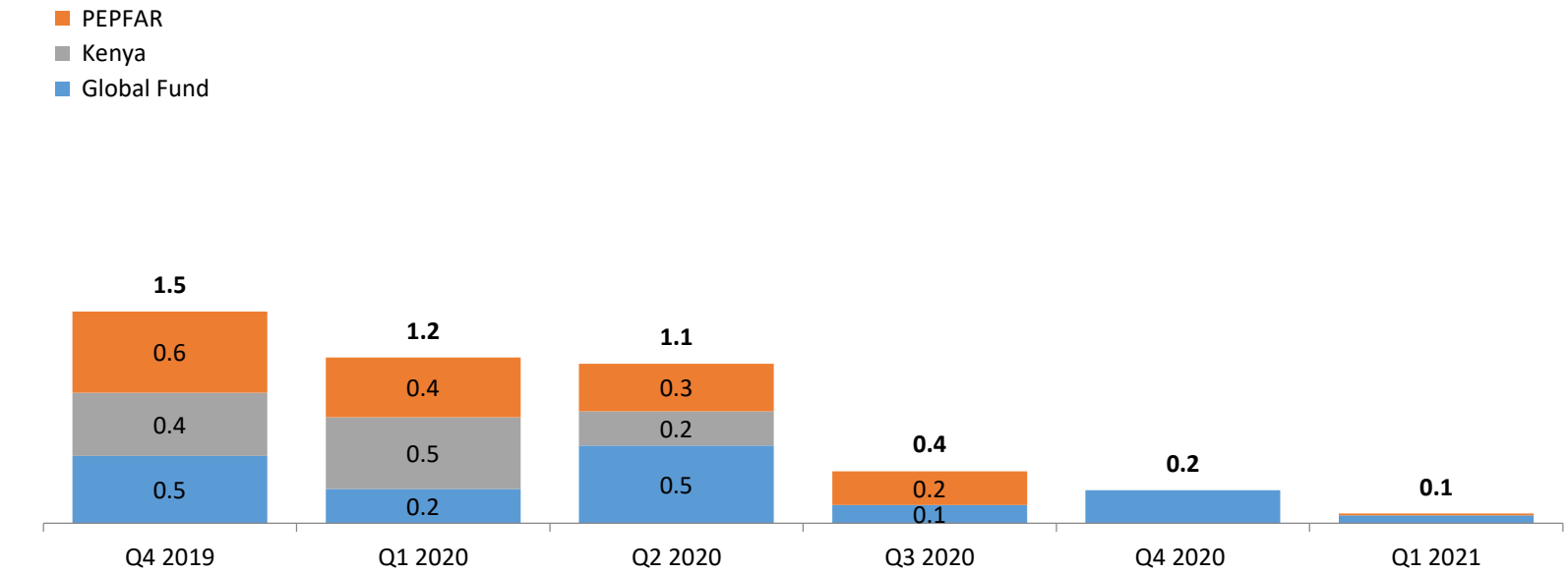
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

ATV/r 300/100 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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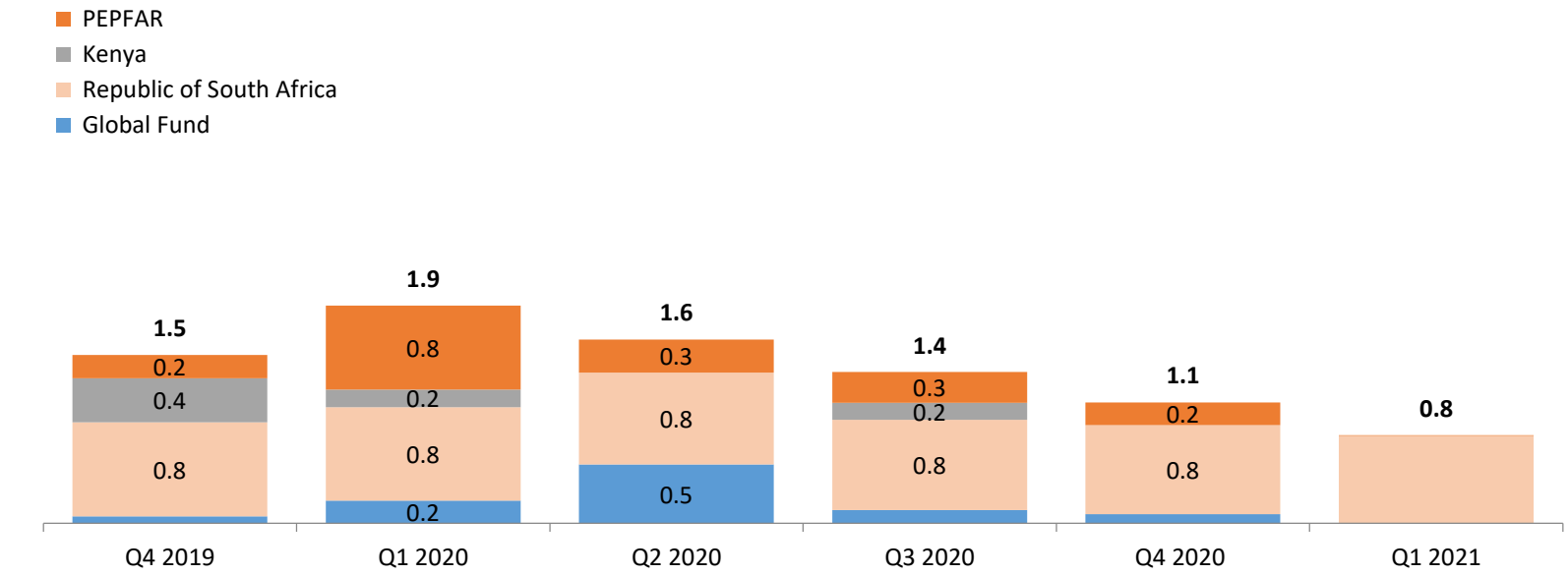
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

LPV/r 200/50 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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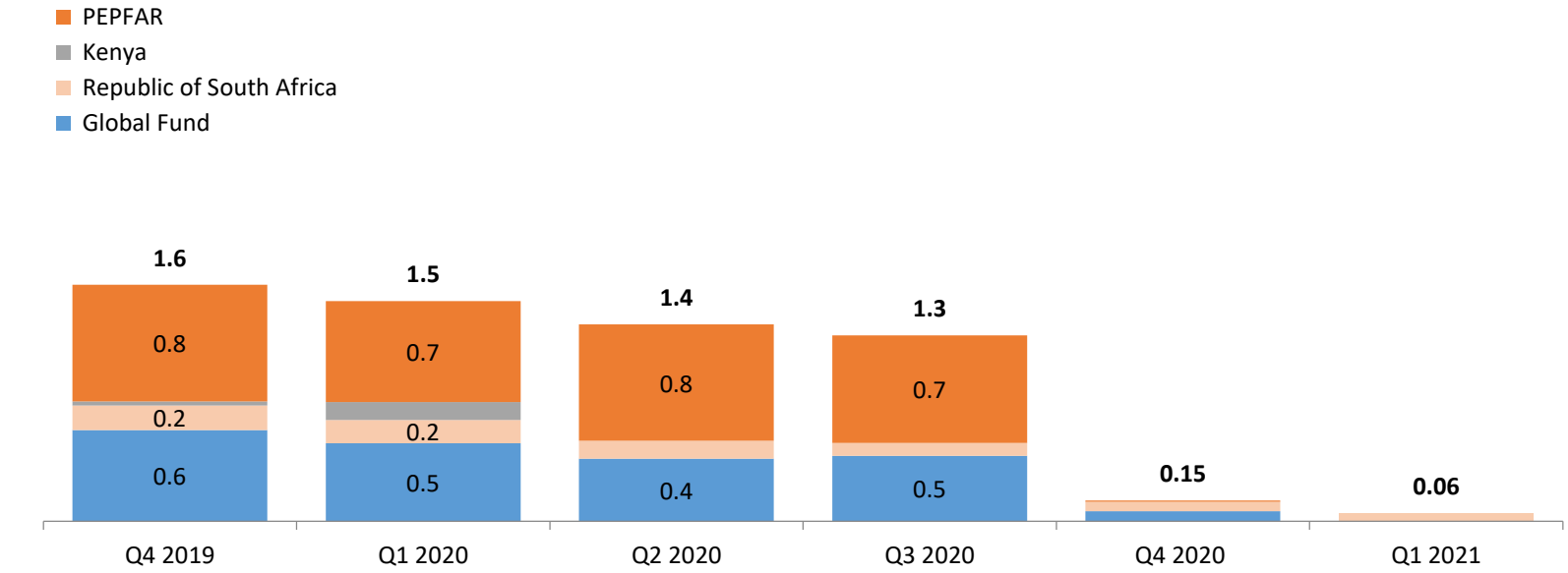
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

LPV/r 100/25 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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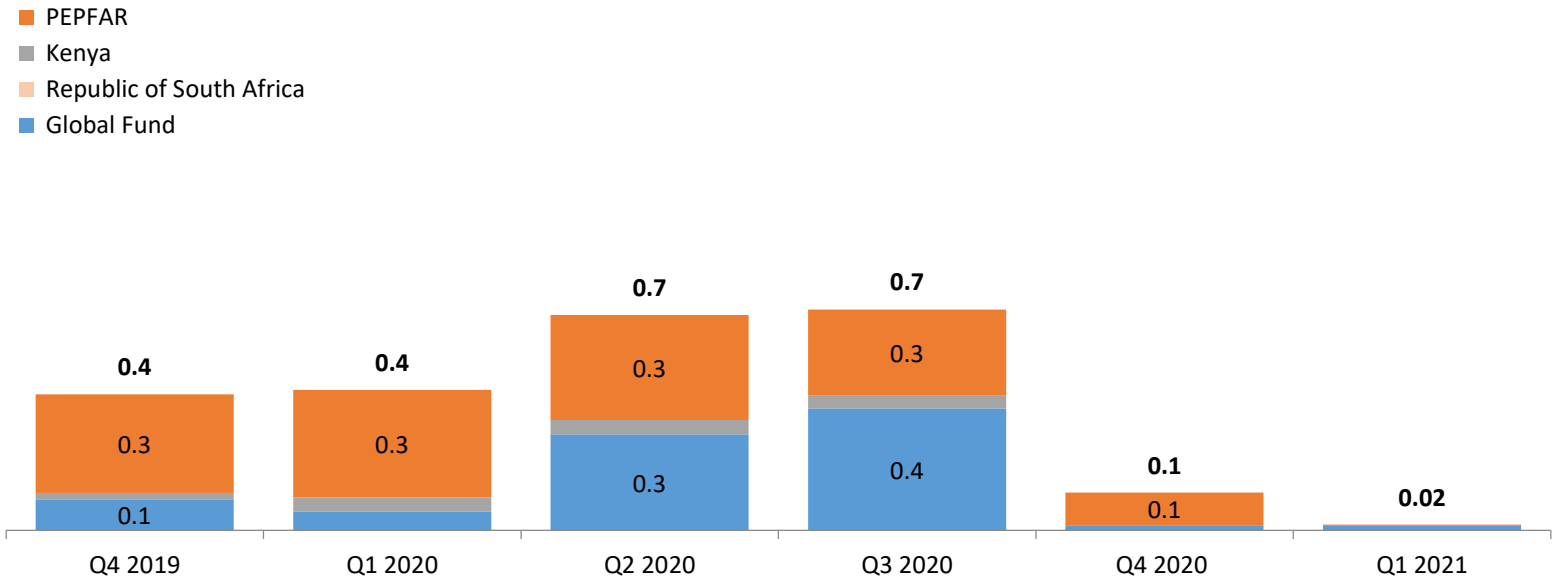
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

LPV/r 40/10 Capsules/Granules – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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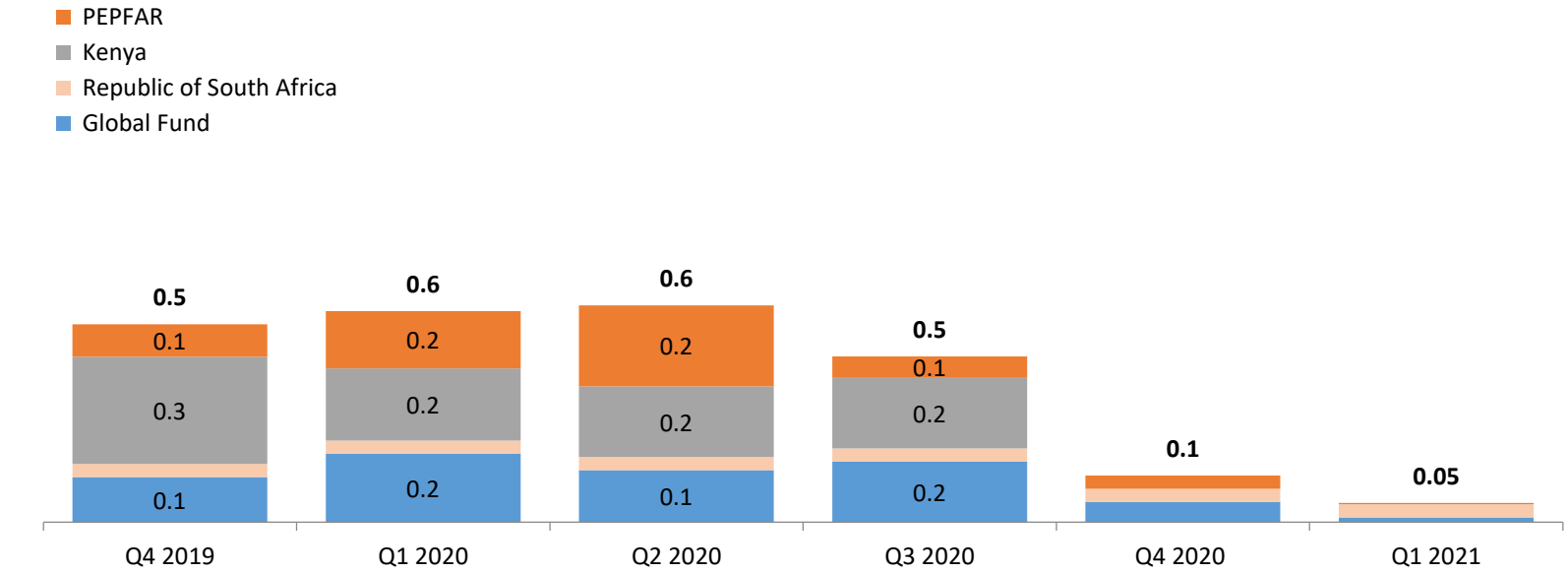
SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

NVP 100ml Oral Suspension – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook

Q4 2019-Q1 2021, Number of packs, millions



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SOURCE: PEPFAR, Government of Kenya, The Global Fund, South Africa

Supply Chain Optimization

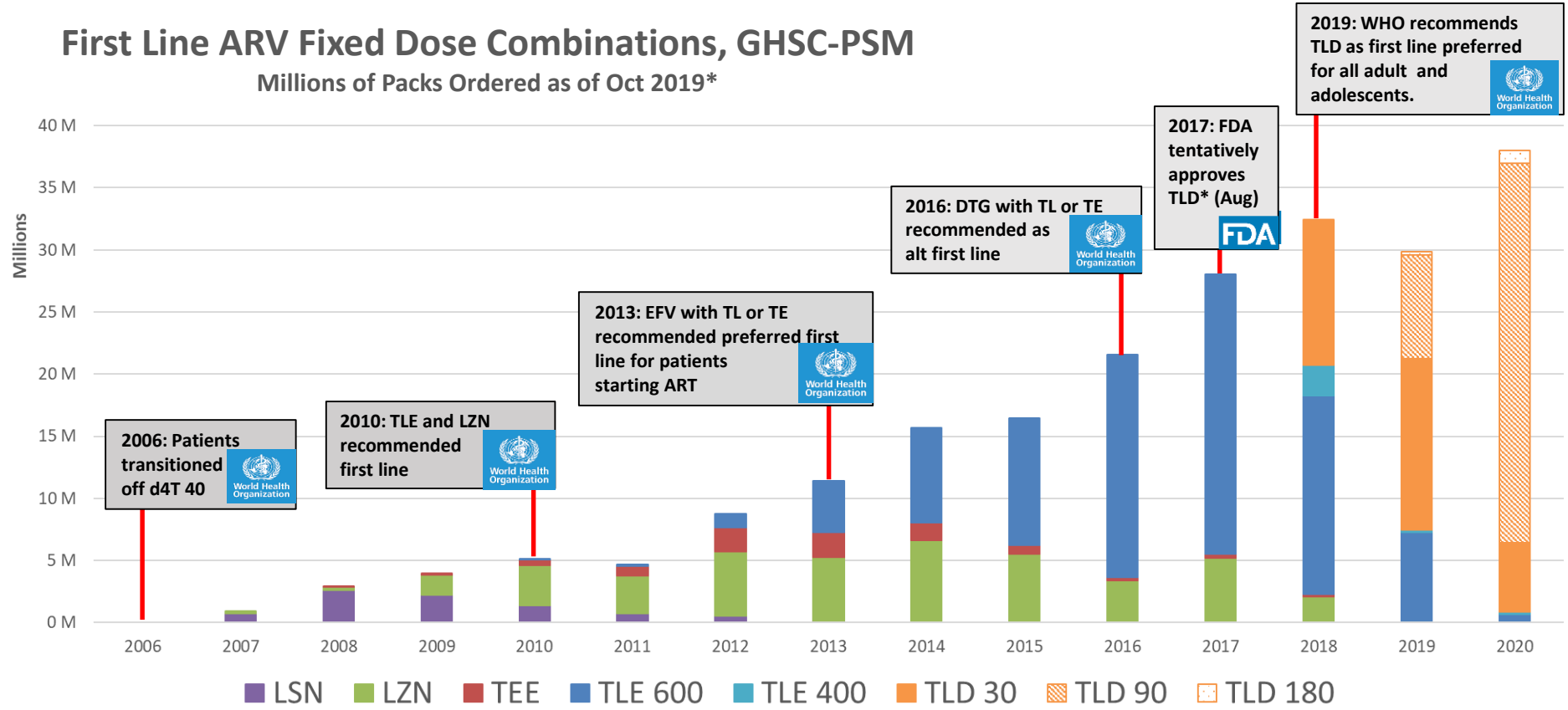
Christine Y. Malati, Pharmaceutical Adviser

2019 Annual ARV Buyer Seller Summit

Washington, DC, USA

November 25 – 27, 2109

Pace and Magnitude of Adult First Line Transitions



USAID FROM THE AMERICAN PEOPLE

*All TLD packs shown are in equivalent units of 30 tablet packs. For example, one pack of TLD 90 tablet count equals three packs of TLD 30 tablet count.

Illustrative Elements of Patient-Centered Care in the Clinical Cascade

1st 95

- Specialized services for priority populations (AGYW, men, KP, OVC)
- Community based services delivered to the client
  - HIV self testing
  - PrEP

2nd 95

- TLD transition and reduction of legacy product
- Treatment literacy, pre-ART and initial adherence counseling
- Multi-month distribution

3rd 95

- Decentralized distribution of treatment closer to client, external pick up points
- Adherence support (social support, refill reminders)
- U=U

- Optimizing workflow for service efficiency
  - Reducing wait times, and streamline organization of files, team-based provider approaches
- Systems - active patient tracing, improving record keeping
- Accelerated utilization of the private sector to meet client needs for expanded access to services and commodities

80

From a presentation by Polly Dunford's Nov 2019 (Johannesburg)

Benefits of Decentralized Drug Distribution (DDD)

- Retention, adherence & viral load suppression:
  - Men prefer the private sector (hours & perceptions about public facilities)
  - Faster pickup points
  - Lower transport costs to patients
  - Decanting to private pickup points lets ART sites focus on the sickest patients
  - Stigma less of a barrier for discrete drug pick-up

Examples of DDD Models

Automated (eLocker/ATM)

High capital costs (esp. ATMs), need high utilization and quick pickup to be cost effective

Suited to urban, high volume sites

Requires integration with broader chronic care medication

Community Pharmacy

Uses existing infrastructure and HRH

Suited to urban and peri-urban

Fee-for-service models highly sustainable

Nurse-managed private clinic

Community-based

Can use existing clinic infrastructure or pop-up mobile outlets (above)

Opportunity to add other HIV services and integrate with other primary care

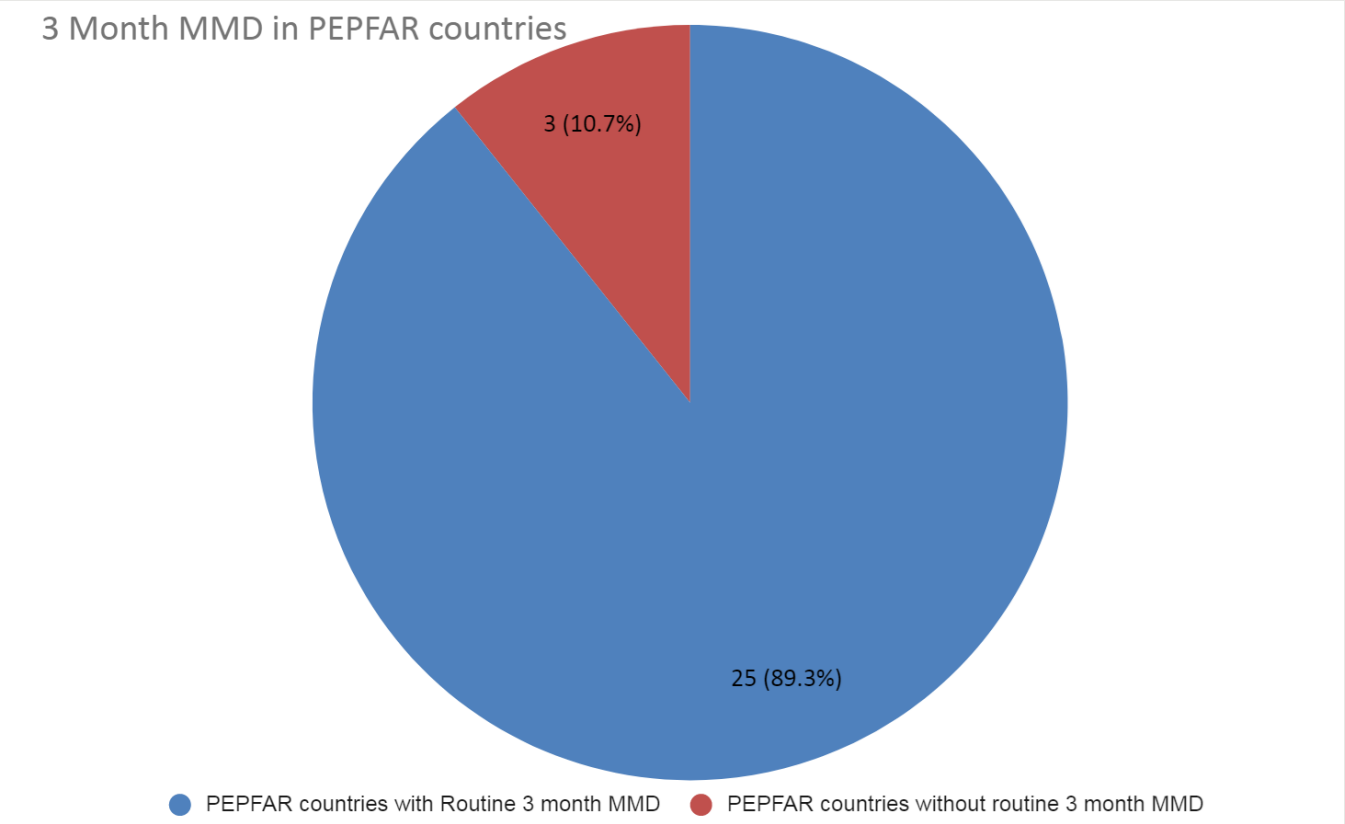
Image credit from left: RightePharmacy, SIDHAS FHI360 Nigeria, Sha'P Left Cipla Foundation

Supporting Clinical Treatment Implementation with Optimization of the Supply Chain – MULTI MONTH DISPENSING

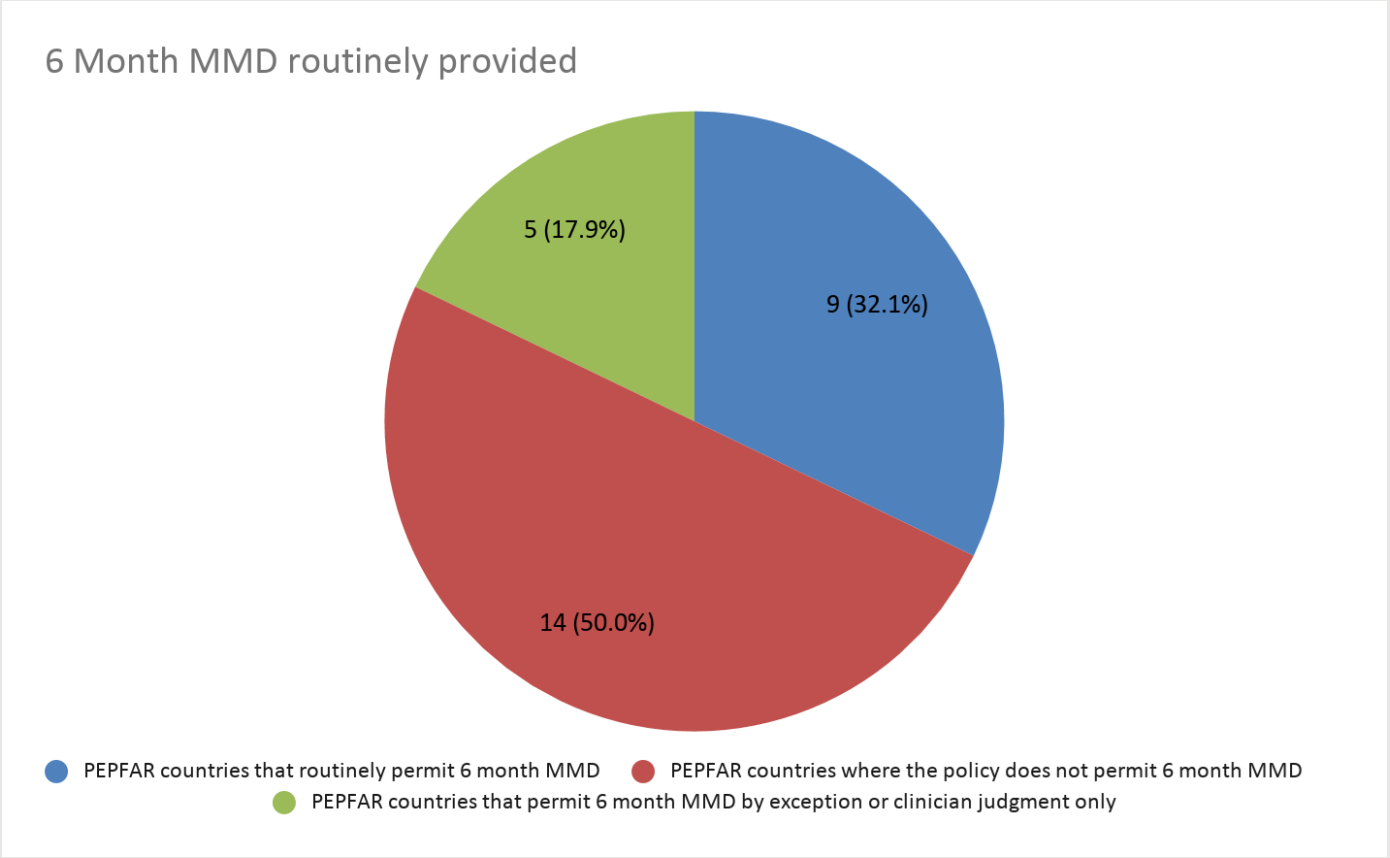
Multi Month Dispensing Short Term Task Team

- Ensuring availability of policy to drive eligibility criteria
- Utilization of larger count bottles of first line
  - 90 and 180 count packaging of TLD
  - 90 count packaging of TLE400 and ALD
- Ultimately using MMD principles for pediatric treatment once security of pediatric formulations can be enhanced

PEPFAR Countries with 3+ Month MMD policies

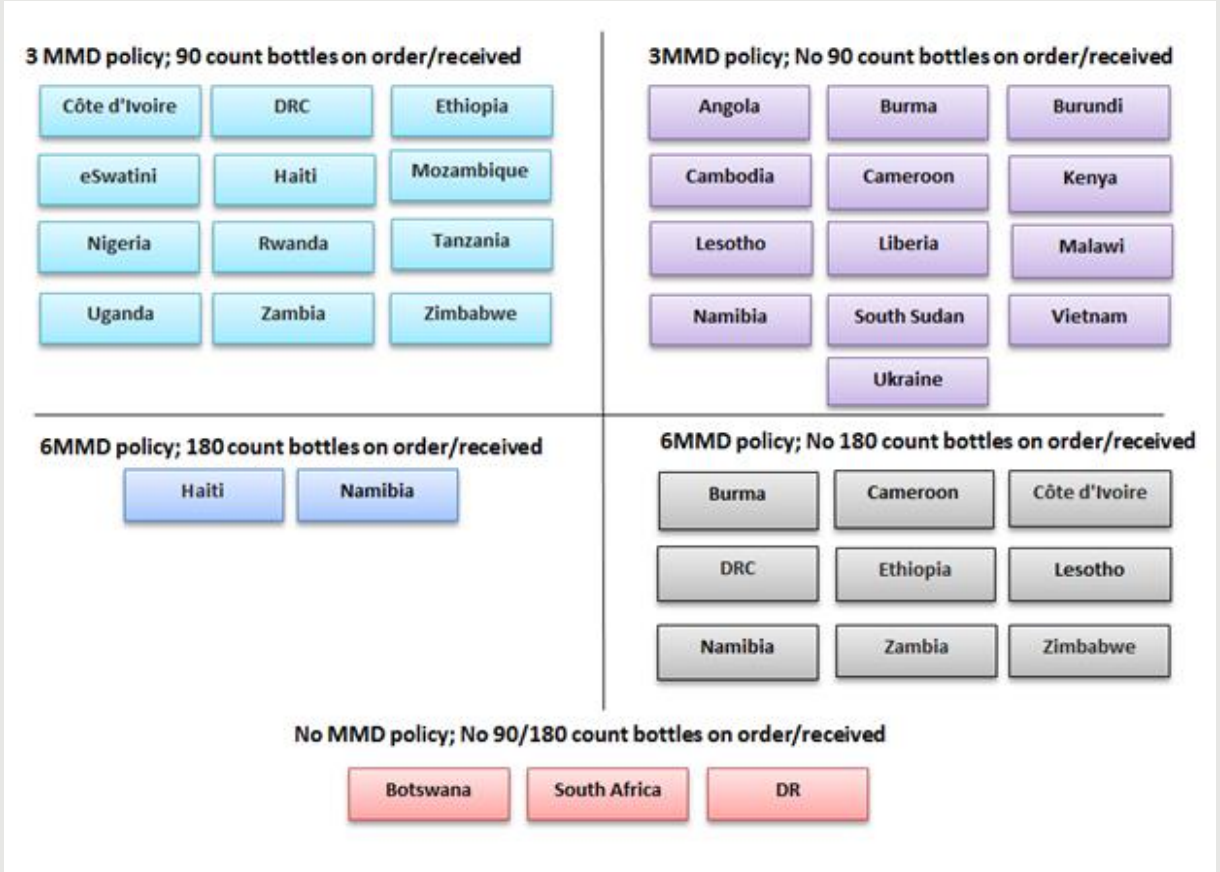


PEPFAR Countries with 6 Month MMD policies



OUs	3 month MMD	6 month MMD	Comments
Botswana, the DR, and South Africa	No	No	These three countries do not presently support MMD. All three have draft policies.
Angola, Burundi, Liberia, Mozambique, Rwanda, South Sudan, eSwatini, Tanzania, Uganda, and Ukraine	✔	No	Policies in these countries do not permit MMD greater than 3 months. Many of them they do permit MMS.
Cambodia, Kenya, Malawi, Nigeria, and Vietnam	✔	Sometimes	6 month MMD is largely at the discretion of the clinician involved.
Burma, Cameroon, Côte d'Ivoire, DRC, Ethiopia, Haiti, Lesotho, Namibia, Zambia, Zimbabwe	✔	✔	These countries offer 3-6 month MMD and sometimes more than 6 month MMD.

MMD Policy vs. Supply Chain



Nigeria

Projected Consumption Breakdown for Patients (TLD 30 Tab vs. TLD 90 Tab)

***Data source**: ARVs/OI medicine Supply Plan (Pipeline), 27 Sept 2019.*

***Notes**:*

- *To enable comparison of consumption by patients across packaging size; 90 tab/bottle consumption multiplied by 3 to enable aggregation with 30 tab/bottle*

TxNew:

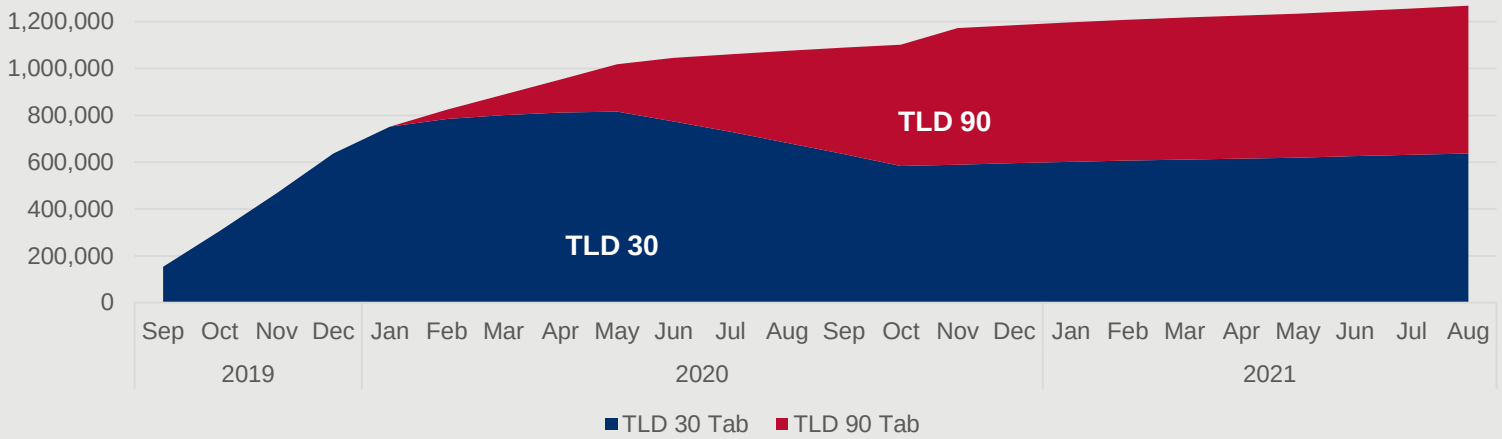
- PEPFAR COP19 TxNew target is 379,707. National TxNew target is 425,784.
- The projected 425,784 TxNew patients are expected to consume 5 million of TLD30 or 1.7 million packs of TLD90 in one year.

TxCurr:

- Adult first line TxCurr is 1,119,977 as of August 2019 (data source: Federal Ministry of Health patients per regimen report).
- It is projected that 91% (1,019,179) of this adult first line TxCurr will be using TLD regimen post transition. This translate to 12 million packs of TLD 30 or 4 million packs of TLD90

Mozambique

Projected Consumption Breakdown for Patients (TLD 30 Tab vs. TLD 90 Tab)



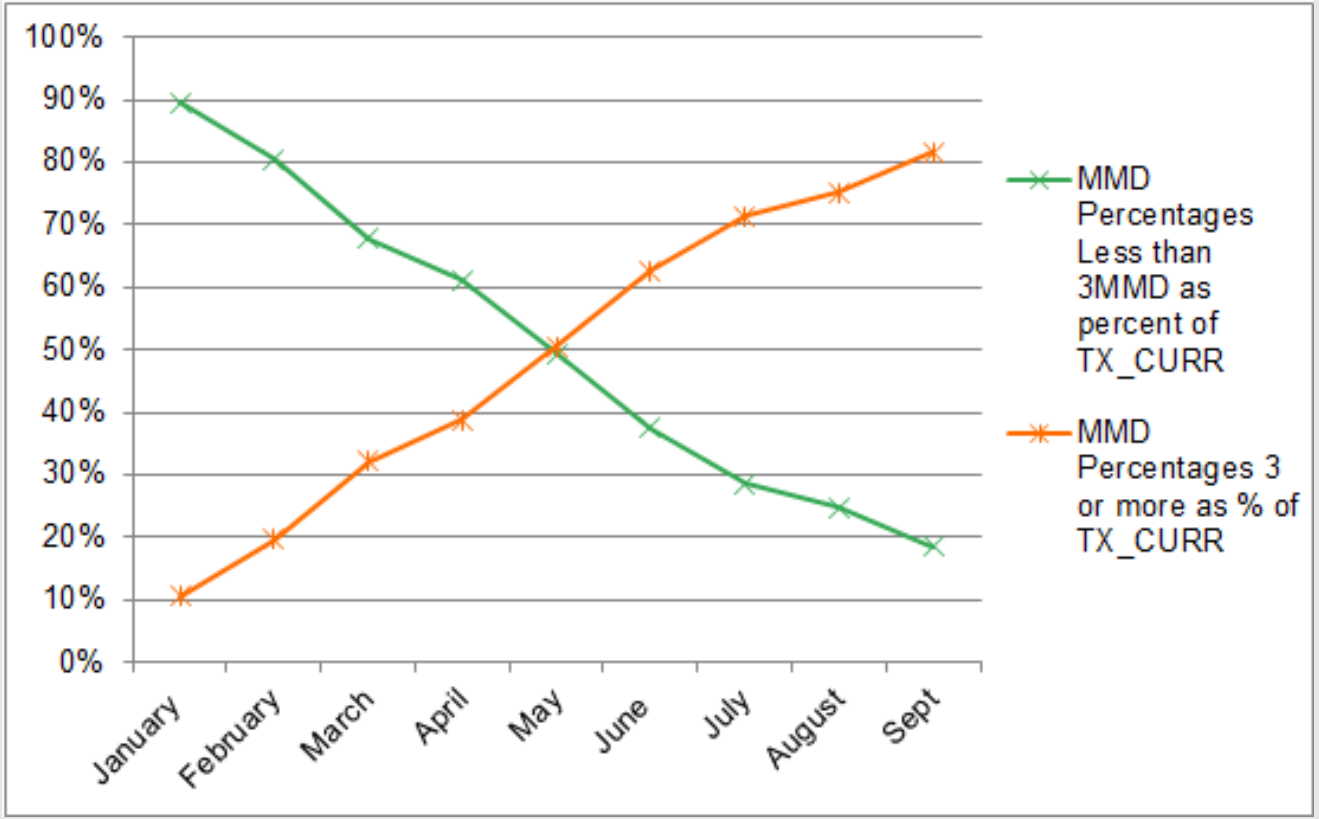
***Data sources**:*

- *Estimated consumption: TLD transition forecast tool; Actual consumption: LMIS - MMIA – aggregated monthly consumption reported per SDP*

Notes:

- *To enable comparison of consumption by patients across packaging size; 90 tab/bottle consumption multiplied by 3 to enable aggregation with 30 tab/bottle*
- *TLD 30/90 use to be review with 6MDD fast expansion – TLD 90 consumption should increase significantly*

MMD as a percent of TX_CURR



Collaboration between USAID and WHO / Essential Medicines Programme to develop recommendation for shelf life importation requirements

Supply chain shelf-life regulations for health commodities

Problem Description:

- In many instances current regulations have proven to hinder importation of life saving medical products and adversely impact patient access.
- Consumption patterns in many countries often requires far less SL than the those mandated by regulations requiring a minimum percentage SL (ex. 75% RSL).
- Many countries have made significant improvements in forecasting and supply chain management.
- Rejection of products due to the requirement of a minimum percentage of RSL may contribute to stockouts.

Supply chain shelf-life regulations for health commodities

Maximum SL	75% RSL	80% RSL	85% RSL
24 months	18 months	19.2 months	20.4 months
36 months	27 months	28.8 months	30.6 months
48 months	36 months	38.4 months	40.8 months
60 months	45 months	48 months	51 months

USAID is collaborating with WHO to develop a recommendation on importation requirements

- Scope includes pharmaceuticals, vaccines and medical devices (including in vitro diagnostics and reagents/components).
  - Excludes “kits” (ex: VMMC kits)
- Recommends shift from requiring a minimum percentage of RSL to a months-based RSL importation policy.
- Expected to be reviewed by WHO ECSPP in Oct 2019.

WHO Working document QAS/19.788/Rev.1available at :
https://www.who.int/medicines/areas/quality_safety/quality_assurance/QAS19_788_Rev1_Remaining_Shelf_Life_of_Medical_Products.pdf

The policy allows for flexibility dependent upon consumption rates

Expiry date	RSL at time of dispatch from Manufacturer's premises	RSL at time of delivery at port of entry of country	RSL at time of delivery at point, after customs clearance	RSL at time of delivery at end-user level
48 months < RSL < 60 months	40 months	30 months	18 months	12 months
36 months < RSL < 48 months	30 months	24 months	18 months	12 months
24 months < RSL < 36 months	20 months	15 months	10 months	6 months
12 to 24 months	9 months	7 months	5 months	3 months
Less than 12 months	Special arrangements and conditions apply			

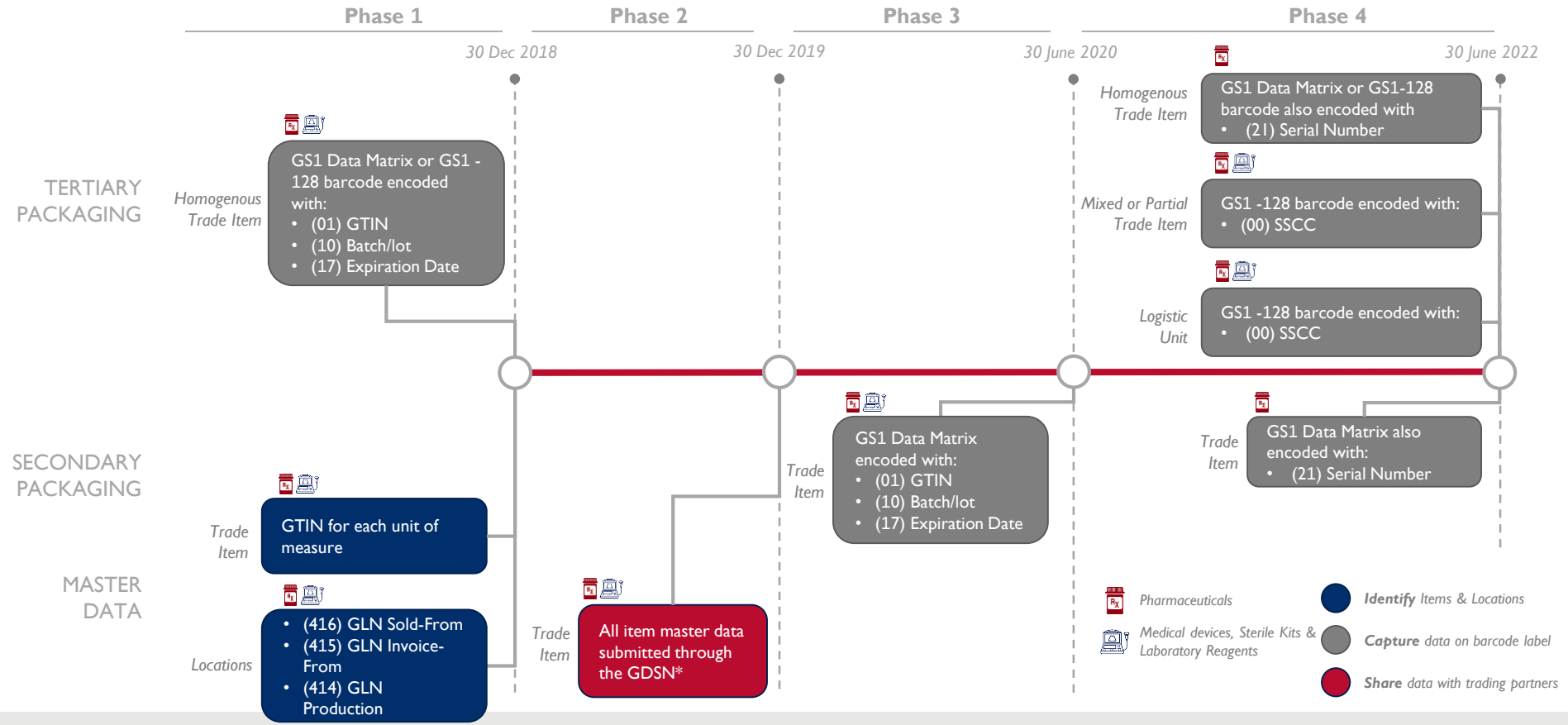
Benefits of a Months-Based RSL Importation Policy include the following

Increases the efficiency of global public health supply chains to help ensure patients do not receive expired products

- Incentivizes manufacturers to file for longer SL
- Removes potential preferences of procuring lower SL products
- Aligns practices in supply chain management of (stock on hand in terms of months of supply) with import regulations
- Decrease use of exceptions and allow for more predictable importation process

Updates on GS1

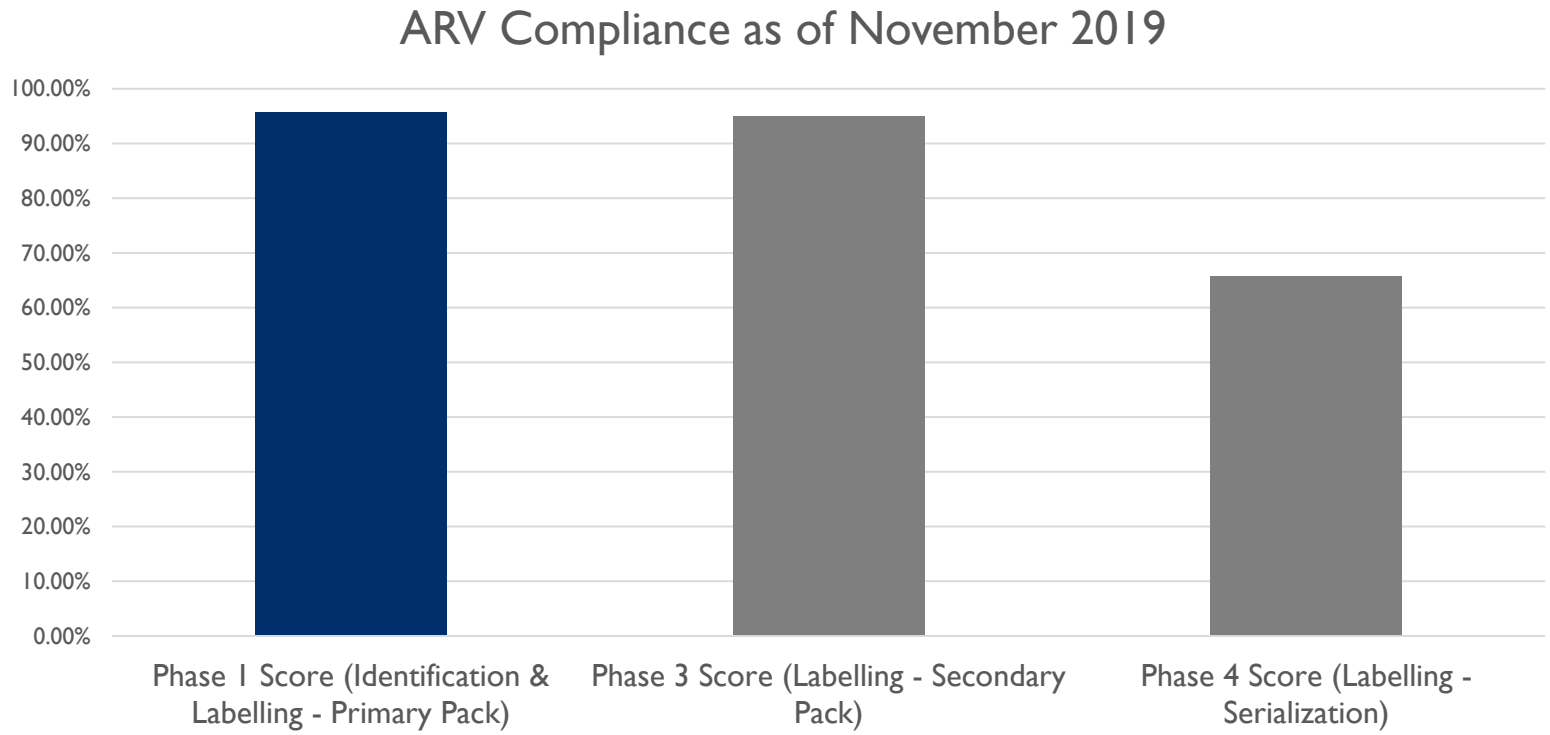
GHSC-PSM GS1 Global Standards Requirements



*For more information on how to comply: www.1worldsync.com/customer-page/ghsc-psm
For more information on our requirements: https://gs1supplychain.org/globalstandards

GTIN: Global Trade Item Number **GDSN**: Global Data Synchronization Network
GLN: Global Location Number **SSCC**: Serial Shipping Container Code

Compliance to date: Identification & Labelling



Suppliers synchronizing through GDSN

USAID Global Health Supply Chain Program

2018-2019 Timeline for Compliance

1

Identification & Labeling

- Allocate GTINs & GLNs for all items & locations
- Complete GTIN & GLN Submission Form HERE
- Provide tertiary pack label samples to datasync@ghsc-psm.org

DEADLINE
30th December 2018

2

Register for Data-pool

Data-pools are the mechanism for sending GTIN master data to GHSC-PSM

Find List of GS1-Certified Data Pools at https://www.gs1.org/services/gdsn/certified-data-pools

RECOMMENDED
March-June 2019

3

Publish Content to GHSC-PSM

- Email datasync@ghsc-psm.org to say that you are ready to synchronize data
- Review attribute requirements
- Publish
- Maintain!

DEADLINE
30th December 2019

Serialization

- Serialization roadmap currently under development
- Organizations coordinating on vision:
  - ✓ USAID
  - ✓ USAID Nigeria
  - ✓ USAID Ethiopia
  - ✓ Global Fund
  - ✓ GS1 Global Office
  - ✓ USAID GHSC-PSM
  - ✓ eHIS
  - ✓ *…and more*

Supply Chain Optimization

Christine Y. Malati, Pharmaceutical Adviser

2019 Annual ARV Buyer Seller Summit

Washington, DC, USA

November 25 – 27, 2109

ARV Large Buyer Seller Summit: Stock tracking

Republic of South Africa

Ms Khadija Jamaloodien
Affordable Medicines Directorate

ARV Large Buyer Seller Summit
November 2019
Day 3

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Contents

ARV stockouts make headlines in SA

The Citizen

newsletter competitions

News Parenty Business Sport Phakaaathi Lifestyle Travel Motoring

health 5.6.2019 07:51 pm

Global ingredient shortage behind ARV stockouts in SA

nam aidsmap
HIV & AIDS – sharing knowledge, changing lives

Access to medicines & treatment

High prevalence of stockouts of antiretroviral medicines in South Africa

Alain Volny-Anne | 23 May 2019

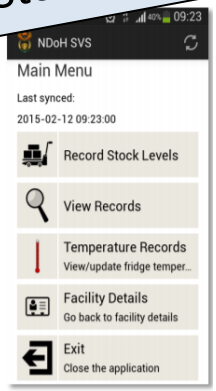
ARV stockouts putting lives at risk, says SSP

STOP STOCKOUTS

4th June 2019 | Anso Thom

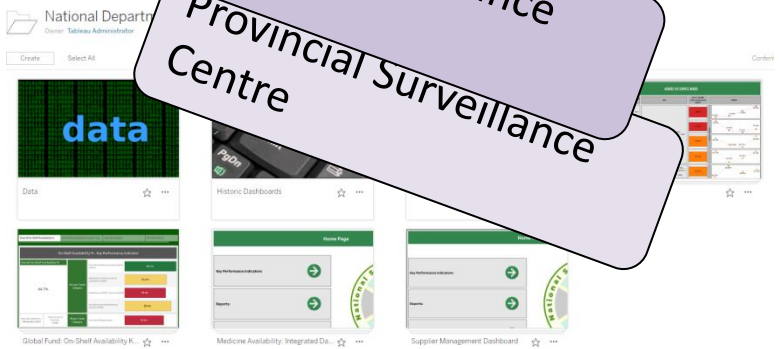
Over recent years the NDoH has made strides in supply chain planning

Stock visibility system



National Surveillance Centre

Provincial Surveillance Centre

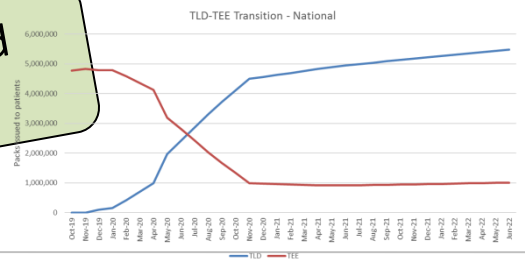


Alternative distribution channels (CCMDD, GP Care Cell, Automated dispensing solutions)

GP Care Cell Programme

Demand & supply planning

TLD transition detailed planning



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SA has automated visibility of a number of KPIs

tableau | Search | RB

Explore / National Department of Health / AMD Scorecard / AMD SCORECARD ☆ | Data Sources

Undo | Redo | Revert | Refresh | Pause | Subscribe | Share | Download | Comments | Full Screen

AMD SCORECARD

	KPI:	TARGET:	KEY:	AS- IS - SCORE: *(Hover to see more detail)*	TREND:
MEDICINE AVAILABILITY KPI's	DEPOT AVAILABILITY	90%	GREEN: Medicine Availability % > 90% AMBER: Medicine Availability % < 90% but > 80% RED: Medicine Availability % < 80%	77,91%	WEEKLY TREND: 77,07% → 77,83% → 78,60%
	CCMDD AVAILABILITY	90%		68,26%	74,70% → 73,72% → 75,28%
	HOSPITAL AVAILABILITY	90%		82,28%	82,40% → 82,27% → 82,90%
	CLINIC AVAILABILITY	90%		87,70%	87,27% → 87,42% → 87,70%
CONTRACT MANAGEMENT KPI's	IN FULL:	90 %	GREEN: % of Deliveries delivered in full > 90% AMBER: % of Deliveries delivered in full < 90% but > 80% RED: % of Deliveries delivered in full < 80%	87,53%	MONTHLY TREND: 90,29% → 85,65% → 87,53%
	ON TIME:	90%	GREEN: % of Deliveries delivered on time > 90% AMBER: % of Deliveries delivered on time < 90% but > 80% RED: % of Deliveries delivered on time < 80%	57,67%	66,84% → 57,61% → 57,67%
	ON TIME IN FULL (OTIF):	90%	GREEN: % of Deliveries delivered on time and in full > 90% AMBER: % of Deliveries delivered on time and in full < 90% but > 80% RED: % of Deliveries delivered on time and in full < 80%	55,89%	64,76% → 55,33% → 55,89%
	SUPPLIER CAPACITY:	100%	GREEN: SUPPLIERS can meet demand for 100% of the ITEMS RED: SUPPLIERS can meet demand for < 100% of the ITEMS	79,55%	81,96% → 81,75% → 79,55%
	PAYMENTS OVERDUE:	80%	GREEN: % of Current Debt over Total Debt >80% RED: % of Current Debt over Total Debt < 80%	25,55%	In process of building database to view this

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…with information to facility level

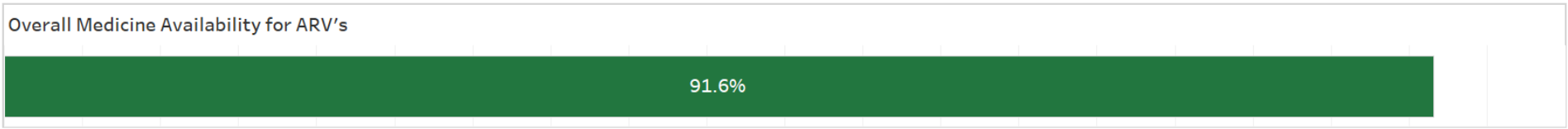
APP: Total number of health facilities reporting stock availability at national surveillance centre

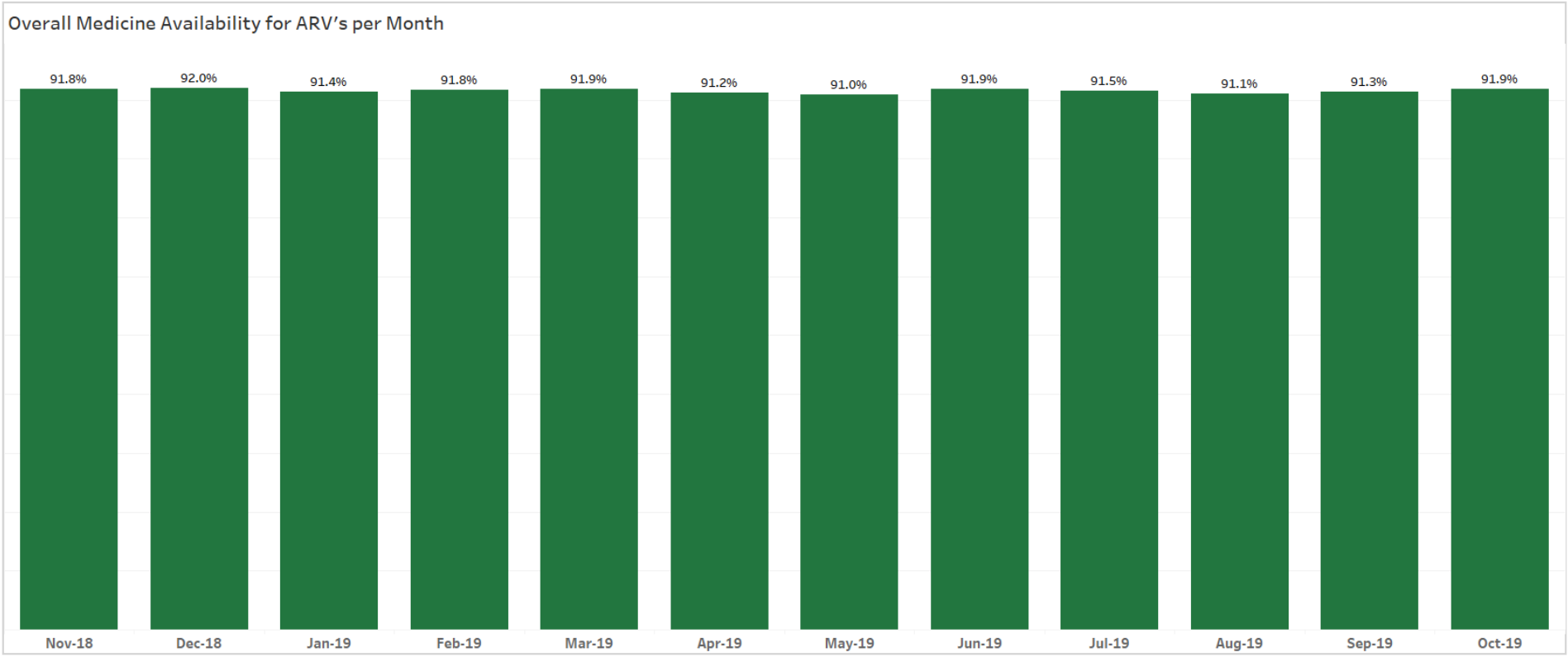
RESULTS: *(Hover for additional information)*

FACILITY TYPE GROUP:	NUMBER OF FACILITIES REPORTING:	2019/20 TARGETS:				2019/20 RESULT:	2020/21
		Q1	Q2	Q3	Q4		
Depot:	23 Facilities	GROUPED 44	GROUPED 44	GROUPED 49	GROUPED 50	GROUPED 176,0%	GROUPED: 1
CCMDD:	8 Facilities						
Other: *GP Carecell / PDU*	57 Facilities						
Hospital:	373 Facilities	340	350	365	385	96,9%	94,
Clinic:	3 272 Facilities	3190	3227	3268	3290	99,5%	98,
TOTAL:	3 733 Facilities	3574	3621	3682	3725	100,2%	98,

FACILITIES SUMMARY:

>90% National Medicine Availability for All ARVs





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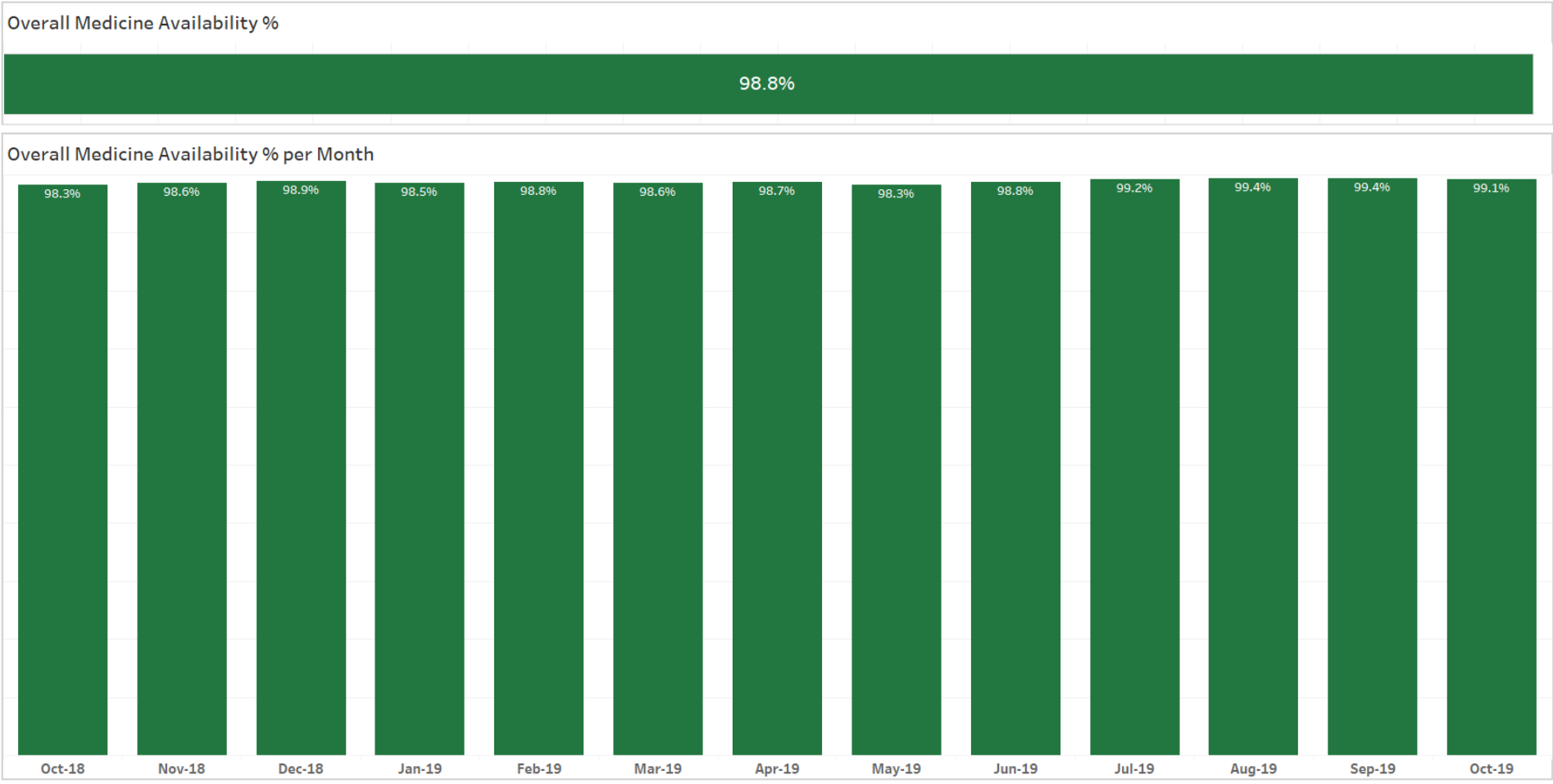
…with TEE 300/200/600 at 99%



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2 provinces require focus

Medicine Availability for All ARVs

Overall Medicine Availability for ARV's per Province

Eastern Cape	Free State	Gauteng	KwaZulu-Natal	Limpopo	Mpumalanga Province	North West Province	Northern Cape
90.8%	92.7%	95.0%	95.2%	84.7%	93.2%	88.6%	93.9%

Overall Medicine Availability for ARV's per Province/Month

	Eastern Cape	Free State	Gauteng	KwaZulu-Natal	Limpopo	Mpumalanga Province	North West Province	Northern Cape
Nov-18	88.6%	91.1%	93.3%	96.2%	88.3%	94.9%	91.5%	94.5%
Dec-18	88.3%	92.1%	93.1%	96.7%	87.8%	96.6%	91.8%	95.1%
Jan-19	87.3%	91.6%	94.6%	96.4%	86.2%	95.4%	90.5%	94.7%
Feb-19	87.8%	92.6%	95.4%	96.3%	86.5%	94.7%	91.3%	94.9%
Mar-19	88.7%	92.6%	95.2%	96.2%	86.3%	94.3%	90.8%	95.4%
Apr-19	91.0%	90.3%	94.8%	95.5%	83.9%	91.1%	88.5%	93.1%
May-19	91.9%	90.5%	94.1%	94.7%	83.6%	91.7%	87.5%	91.8%
Jun-19	93.0%	92.1%	95.9%	94.7%	84.2%	92.6%	88.5%	92.8%
Jul-19	92.9%	94.6%	96.2%	94.0%	82.6%	91.4%	87.5%	94.1%
Aug-19	93.1%	95.0%	96.1%	93.1%	81.8%	90.4%	87.1%	93.8%
Sep-19	93.6%	95.1%	96.7%	93.0%	81.6%	92.4%	85.8%	93.2%
Oct-19	93.4%	94.5%	96.0%	95.4%	83.5%	93.0%	86.0%	93.4%

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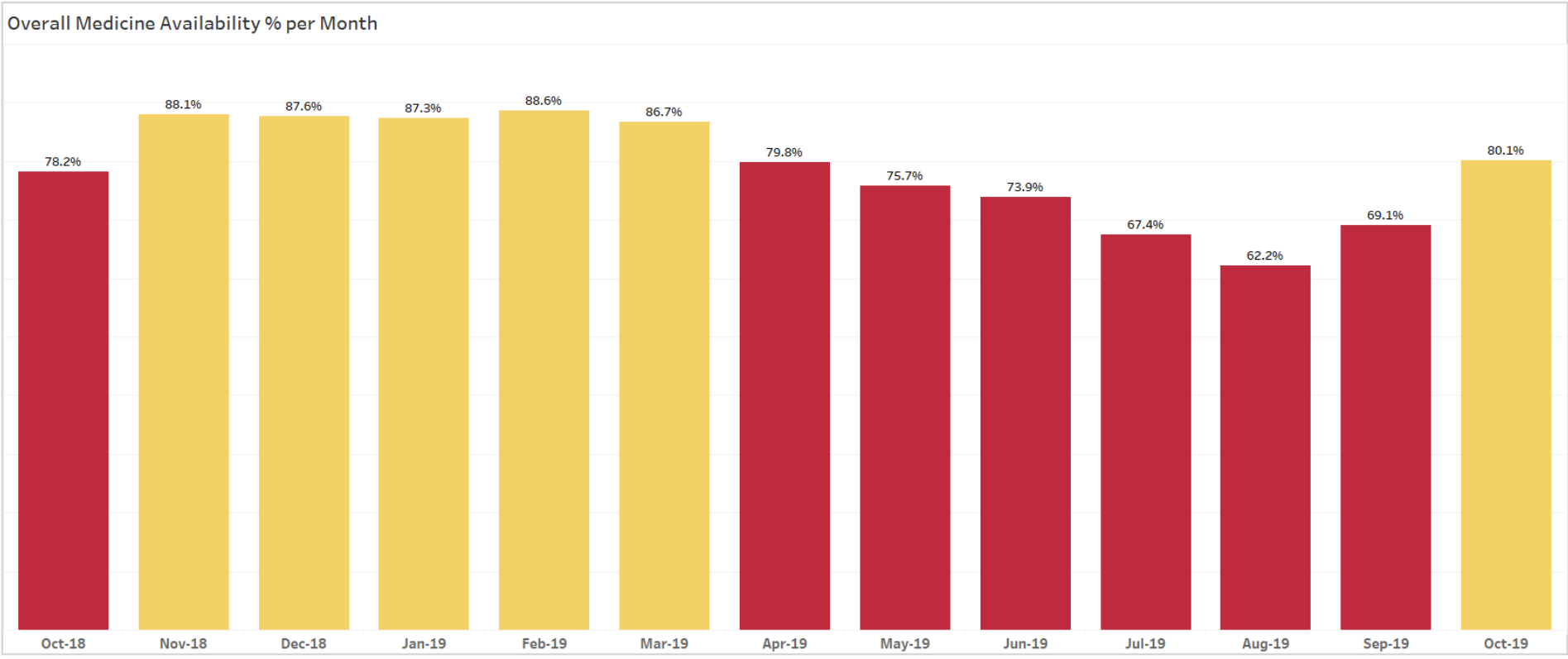
ABC/3TC 600/300 has been a real challenge, but now recovered…



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ABC/3TC 600/300 Provincial Medicine Availability

Provincial Medicine Availability % per Month

	Eastern Cape	Free State	Gauteng	KwaZulu-Natal	Limpopo	Mpumalanga Province	North West Province	Northern Cape
Oct-18	91.2%	49.9%	88.4%	83.5%	74.6%	64.9%		89.8%
Nov-18	90.0%	91.1%	94.0%	88.0%	77.3%	90.5%		94.8%
Dec-18	87.9%	85.9%	92.0%	91.6%	76.7%	90.3%		93.3%
Jan-19	91.0%	85.9%	94.1%	91.6%	74.5%	84.3%		93.3%
Feb-19	94.0%	91.3%	98.4%	90.6%	79.1%	76.6%	100.0%	93.0%
Mar-19	93.5%	88.3%	93.0%	89.1%	80.0%	69.2%	62.5%	92.5%
Apr-19	92.6%	73.1%	84.7%	83.9%	65.4%	61.3%	79.6%	98.2%
May-19	91.8%	68.3%	79.0%	76.5%	60.6%	72.0%	63.9%	
Jun-19	89.5%	82.9%	86.6%	70.7%	58.8%	65.7%	55.7%	
Jul-19	85.1%	93.2%	82.7%	60.9%	45.5%	47.7%	56.9%	
Aug-19	80.5%	81.8%	80.8%	53.8%	44.7%	49.7%	42.0%	
Sep-19	85.1%	90.6%	90.9%	57.8%	45.5%	82.1%	39.3%	
Oct-19	85.4%	96.0%	95.4%	84.1%	58.1%	96.1%	50.8%	

Oct'19: Good recovery in 7 provinces, with 2 still needing to be bolstered

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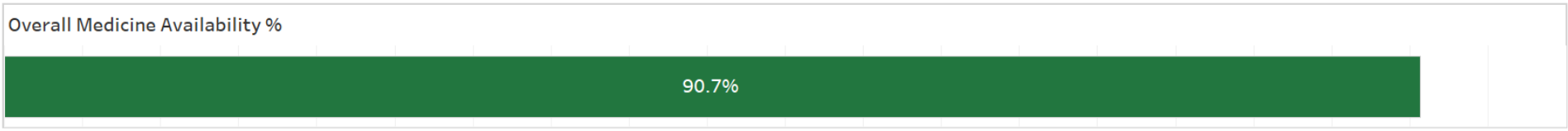
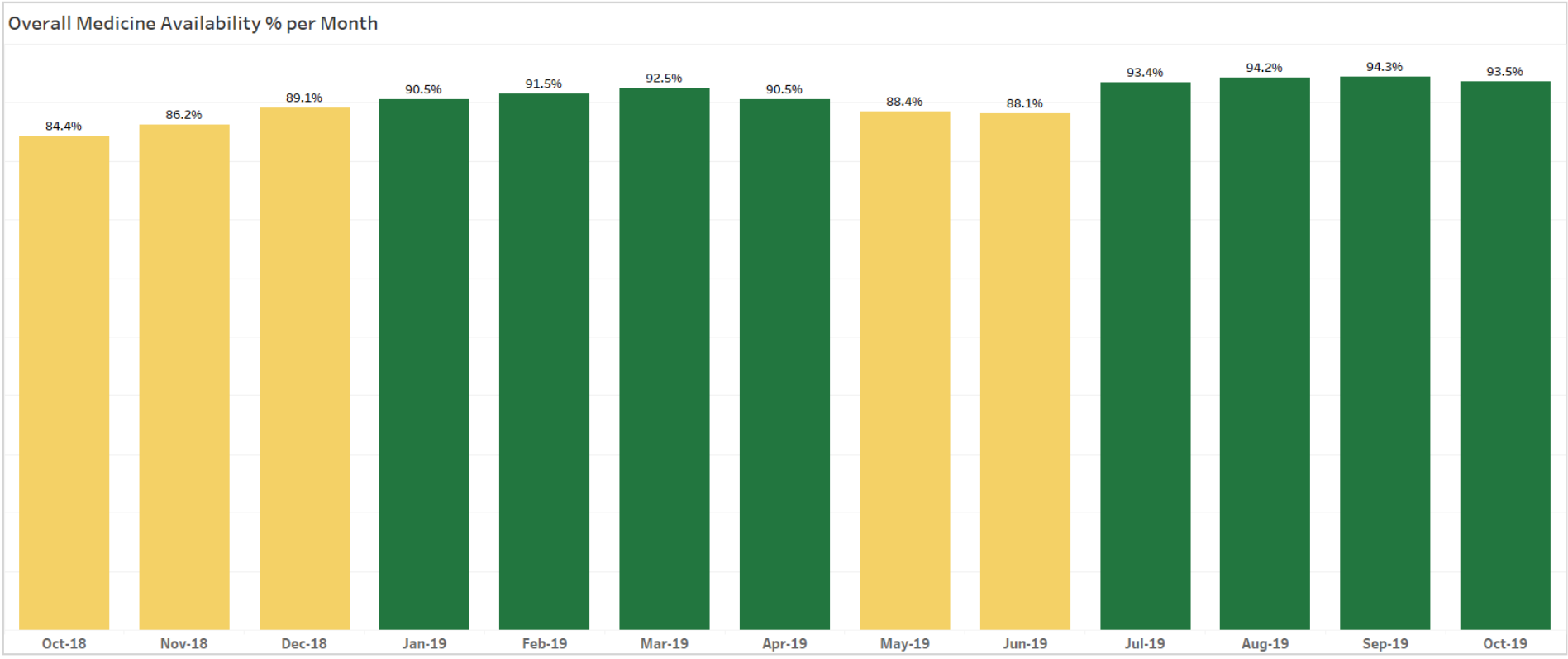
Stockouts in AZT/3TC 300/150 but also stabilised now





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Of concern is a slightly declining trend in supplier performance

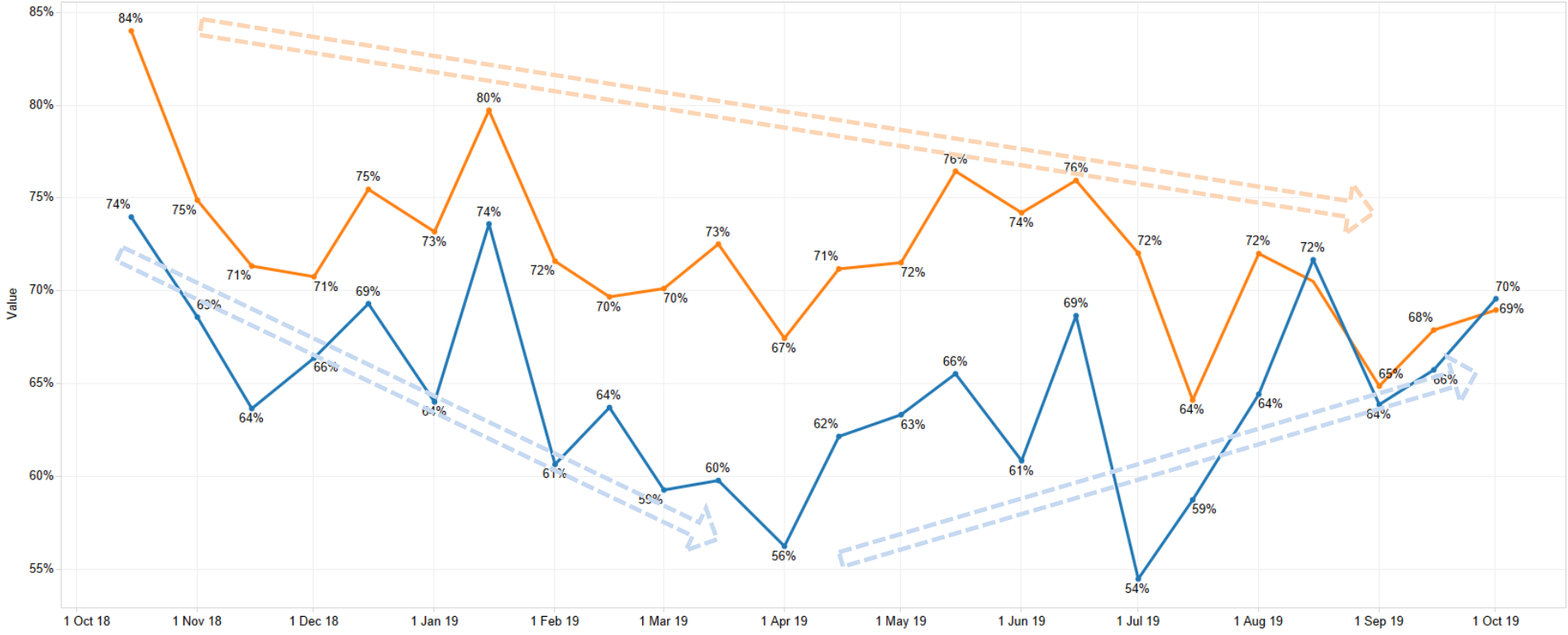
Number of Items

40

Number of Suppliers

12

Ability to Meet Demand and Orders



Measure Names

- Ability to Meet Contractual Demand %
- Ability to Meet Orders %

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Why implement barcoding is SA

According to the World Health Organization (WHO), an estimated **1 in 10 medicinal products** circulating in low- and middle-income countries is either **substandard or falsified**. This means that people are taking medications that either fail to treat or prevent disease or could be harmful. Falsified medical products lead to **a loss of lives**, negatively impact economic growth **and erode overall trust** in the healthcare system.

Track and Trace: Create visibility in the supply chain

Patient safety, security of supply and ***medicine availability*** are of paramount importance within the health sector, and is critical to achieve the desired ***health outcomes.***

The aim is to ensure that the ***correct medicine*** of the ***correct quality*** is available at the ***correct location*** and in the ***correct quantity*** to satisfy ***patient needs***.

Benefits of Track and Trace

Accuracy

Visibility

Inventory management

Improved regulation for all parties

Efficiency

Supply chain security

Recall readiness

Increased revenue for all parties

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Current Legislative & future Contract Requirements

Regulations gazetted 25 August 2017 – Medicines and Related Substances Act (Act 101 of 1965) as amended:

LABELLING OF MEDICINES INTENDED FOR HUMAN USE

10 (1)….the immediate container of every medicine in which a medicine intended for administration to or use by humans is sold shall have a label attached to it on which the following particulars shall appear …..

(n) the lot number of the medicine;

(o) the expiry date of the medicine in a font size that makes it clearly visible;

(p) a barcode suitable for the identification and tracking of medication;

Special Conditions of Contract

"It is mandatory that all products supplied must include a barcode (number plus symbology). All shipper, shelf and unit packs must be marked with the appropriate number and symbology. The European Article Numbering Code 13 (EAN 13) has been accepted as standard.

Suppliers are encouraged to include a 2D barcode or similar on their packaging that will include the following information:

- *Unique identifier (GTIN);*
- *Batch number;*
- *Expiry date."*

Next Steps

- *Develop guideline to be published by SAHPRA which lays down barcoding requirements and timelines*
- Later extend requirements to include medical devices
- Track and trace products throughout the part of the supply chain with appropriate data interchanges and all information stored in a ***central repository***;
- Maintain product integrity from manufacturer to patient for some products

Protect the product

Protect the patients

Contents

“Hot List” process

- Compiled by Contract Management Unit (CMU) by analyzing supplier provided data
- “Hot list” definition:
  - Out of stock items that have longer-term challenges based on analysed data
    - Contracted items
    - Section 21 items
    - Non-awards
- 1st draft Hot List sent and discussed by Improved Medicine Availability Team (IMAT): Monthly and Adhoc if required
- 2nd draft Hot List circulated to the provincial stakeholders prior the monthly teleconference
- Final Hot List is published and submitted to Minister after consensus reached following the teleconference

Hot List content

PRODUCT DETAILS					DEMAND	BACK ORDERS	CONFIRMED STOCK DELIVERIES		
#	Active Pharmaceutical Ingredient	Strength	Pack Size	Supplier	Linear Tender Demand	Total Back Orders	Confirmed Stock Deliveries - Oct	Confirmed Stock Deliveries - Nov	Confirmed Stock Deliveries - Dec

STOCK ON HAND						COMMENTS		
Supplier - Total Stock on Hand	Supplier - Stock in QA	Depots - Total Stock on Hand	CCMDD - Total Stock on Hand	Facilities - Total Stock on Hand	Total Stock in Country	Root Cause	Intervention	Proposed Action

Selected items from Hot List

PRODUCT DETAILS	COMMENTS		
Active Pharmaceutical Ingredient	**Root Cause**	**Intervention**	**Proposed Action**
ABACAVIR and LAMIVUDINE tablet	API Issue (Shortage); High Uptake	Section 21 in place; Partial Deliveries of Registered Stock	Obtain stock on Section 21; Await stock from QA
Isoniazid	High Uptake	Partial Deliveries; Manufacturing Capacity Increased	Facilities to Rotate Stock
Lamivudine	API Issue (Shortage)	Partial Deliveries	Obtain stock on tender from alternate suppliers (Adcock & Pharmacare)
Levonorgestrel , Ethinyl Estradiol, Triphasic	High Uptake; Manufacturing Constraint	Section 21 in place (Alternate pack size)	Obtain stock on Section 21 for alternate pack size (84s)
		Partial Deliveries	Facilities to Rotate Stock
Nevirapine	High Uptake	Partial Deliveries	Obtain alternate pack size from alternate supplier on tender
Norethisterone enanthate	High Uptake (Due to Shortages of Alternate Commodities)	Partial Deliveries; Section 21 in place	Facilities to Rotate Stock
Norgestrel, Ethinyl Estradiol	High Uptake; Manufacturing Constraint	Section 21 in place	Obtain stock on Section 21
Subdermal Implant Containing Etonogestrel	Manufacturing Constraints (Global Capacity Issue)	Partial Deliveries	Facilities to Rotate Stock
Zidovudine	Manufacturing Constraints (Production Capacity)	RFQ Requested	Facilities to Rotate Stock

Contents

Initiatives underway at DoH

- Management processes to be proactive to signals from the National Surveillance Centre (NSC), to manage the supply chain
- Improved demand planning at provincial level, and aggregated at a national level
- Expansion of electronic stock management system footprint and functionality to enhance improve and enhance data provided to the NSC
- Potential for medicine budget to be ringfenced in future years, to ensure availability of funds to pay for medicines ordered
- Improved governance related to Pharmaceutical and Therapeutics Committees (PTCs) to drive better medicine usage, aligned to Standard Treatment Guidelines (STGs) and EML

Request from suppliers

- Accurate reporting of information to the Department of Health via the RSA Pharma portal
- Compliance with contractual terms and conditions
- Maintain contractual stock holding
- Transparency on any issues impacting supply to DoH
- Joint planning with DoH on key SKUs

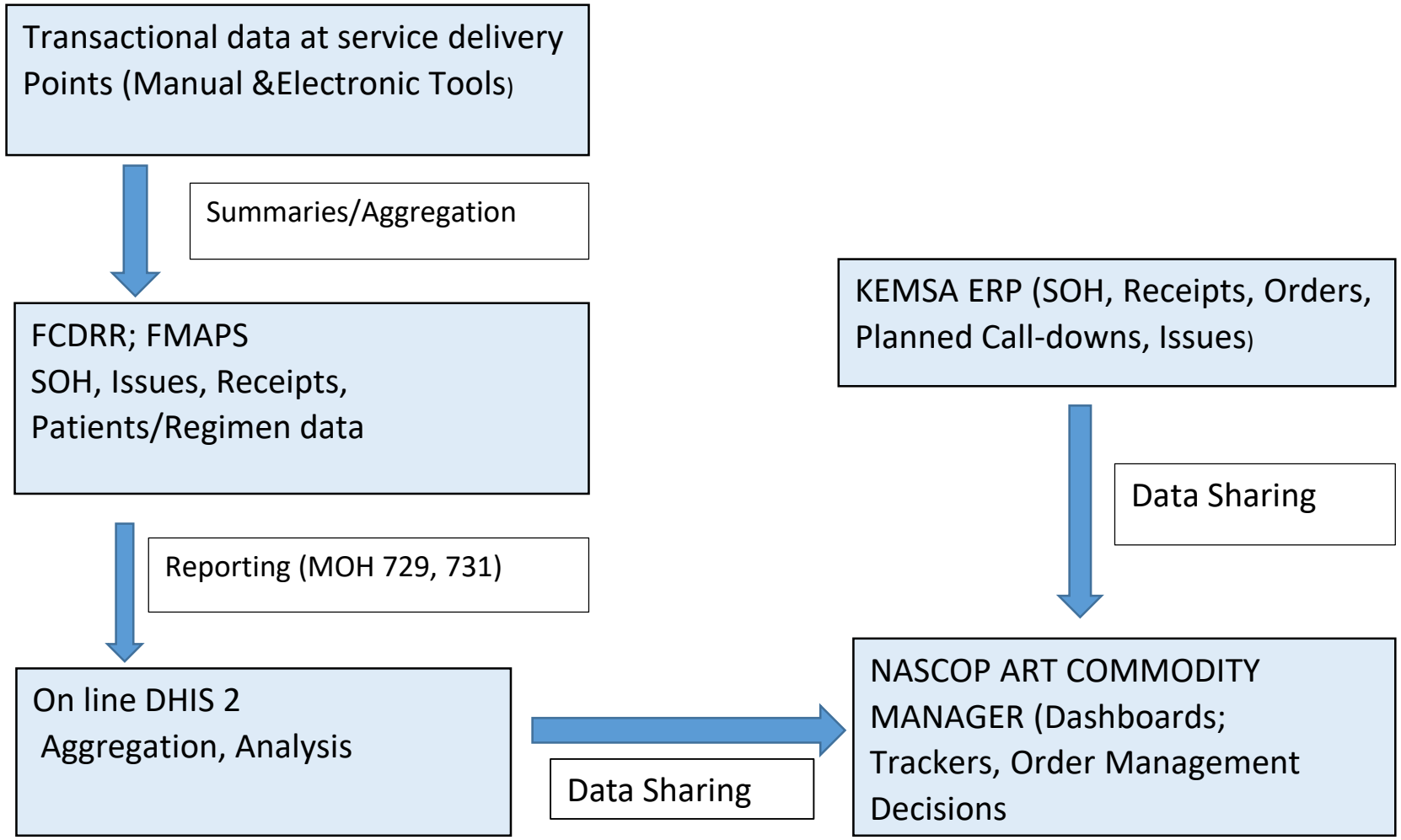
THANK YOU

PEPFAR

U.S. President's Emergency Plan for AIDS Relief

Kenya: Supply Chain Optimization-Data Visibility and Use for Decision-Making

Architecture: Commodity data Reporting, management and Pipeline Monitoring



DHIS2: District Health Information System- Open Source Health Management Data Platform

DHIS2- Facility MoH 731 Form (FCDRR)

Data Set Report

Data criteria | Download as Excel | Download as PDF | Print

Nakuru Provincial General Hospital - September 2019

Completed by: Lmomanyi

Write a comment, question or interpretation of this report

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Adult preparations | Paediatric preparations | Medicines for OIs | TB/ HIV DRUGS

Drug Name	Unit pack size	Beginning Balance	Total Quantity Received this month	Total Quantity Dispensed this month	Losses & Wastage	Pos
		A	B	C	D	
						Ad
Abacavir (ABC) 300mg Tablets	60s	3		23		25
Abacavir/Lamivudine (ABC/3TC) 600mg/300mg FDC Tablets	60s	53	800	497		
Atazanavir/Ritonavir (ATV/r) 300/100mg Tablets	30s	1479	500	472		
Darunavir (DRV) 600mg Tablets	60s					
Dolutegravir(DTG) 50mg tabs	30s	78		39		
Efavirenz (EFV) 400mg Tablets	30s					
Efavirenz (EFV) 600mg Tablets	30s	70		70		

Reported Parameters

- Beginning Balance
- Receipts
- Dispensed
- Losses and Wastage
- Adjustments
- Ending Balance
- Stock<6months
- Order Quantities

DHIS2: MOH 731/ FCDRR Aggregated Data (Kenya)

Data Set Report

Data criteria | Download as Excel | Download as PDF | Print

Kenya - September 2019

Write a comment, question or interpretation of this report

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Adult preparations | Paediatric preparations | Medicines for OIs | TB/ HIV DRUGS

Drug Name	Unit pack size	Beginning Balance	Total Quantity Received this month	Total Quantity Dispensed this month	Losses & Wastage	Posi
		A	B	C	D	
						Ad
Abacavir (ABC) 300mg Tablets	60s	11304	767	1520	8	245
Abacavir/Lamivudine (ABC/3TC) 600mg/300mg FDC Tablets	60s	53716	36106	32236	6	2957
Atazanavir/Ritonavir (ATV/r) 300/100mg Tablets	30s	120323	99512	88633	485	1879
Darunavir (DRV) 600mg Tablets	60s	298	152	185	16	30
Dolutegravir(DTG) 50mg tabs	30s	18239	9672	8041	82	219
Efavirenz (EFV) 400mg Tablets	30s	1381	108	247	2	7
Efavirenz (EFV) 600mg Tablets	30s	36904	2332	4422	462	422
Etravirine (ETV) 200mg Tablets	60s	648	308	326	0	2

DHIS2: MOH 729/F-MAPS Aggregated Data

Data Set Report

Data criteria | Download as Excel | Download as PDF | Print

Kenya - September 2019

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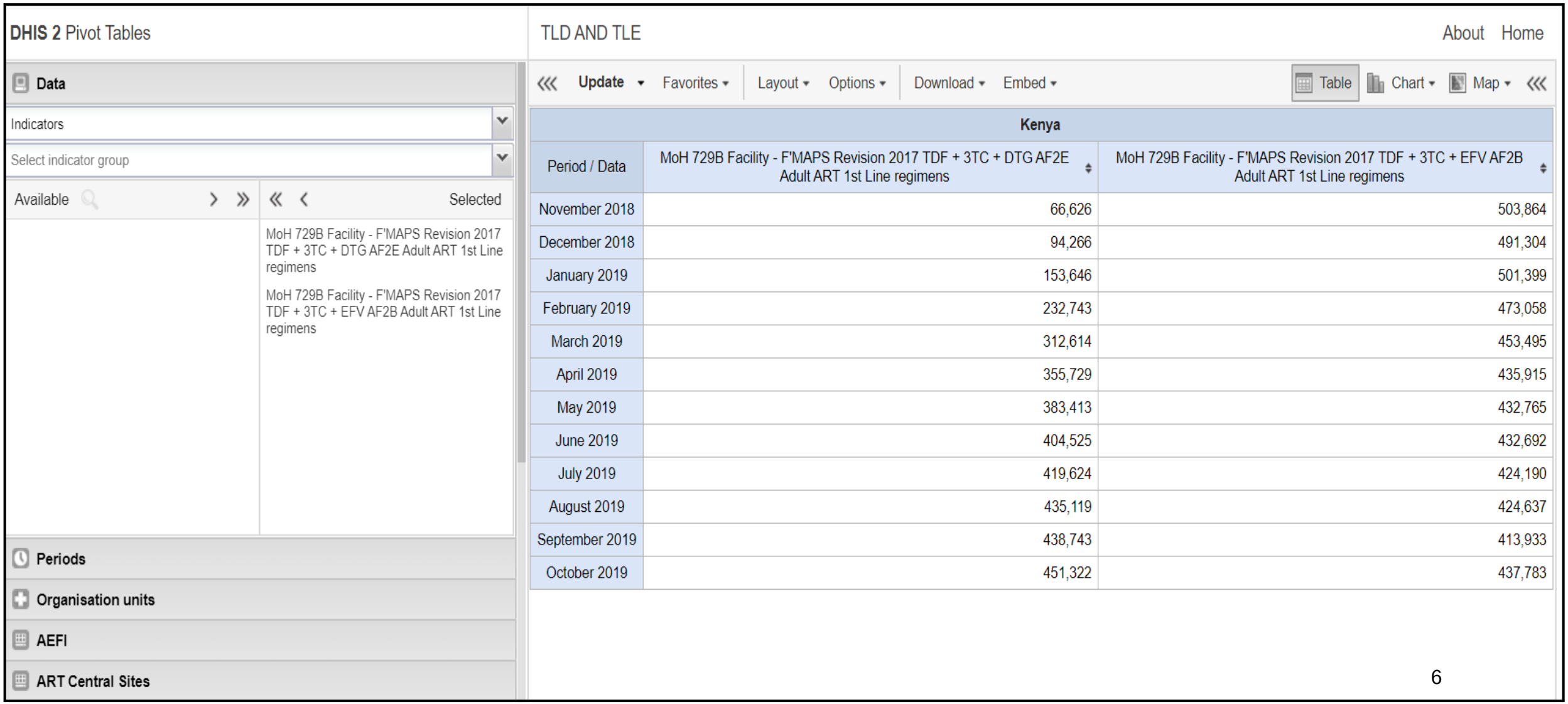
ADULT ART | PAEDIATRIC ART | PMTCT | PrEP | PEP | Hepatitis B Patients who are HIV-ve | Management of Opportunistic infections (OIs)

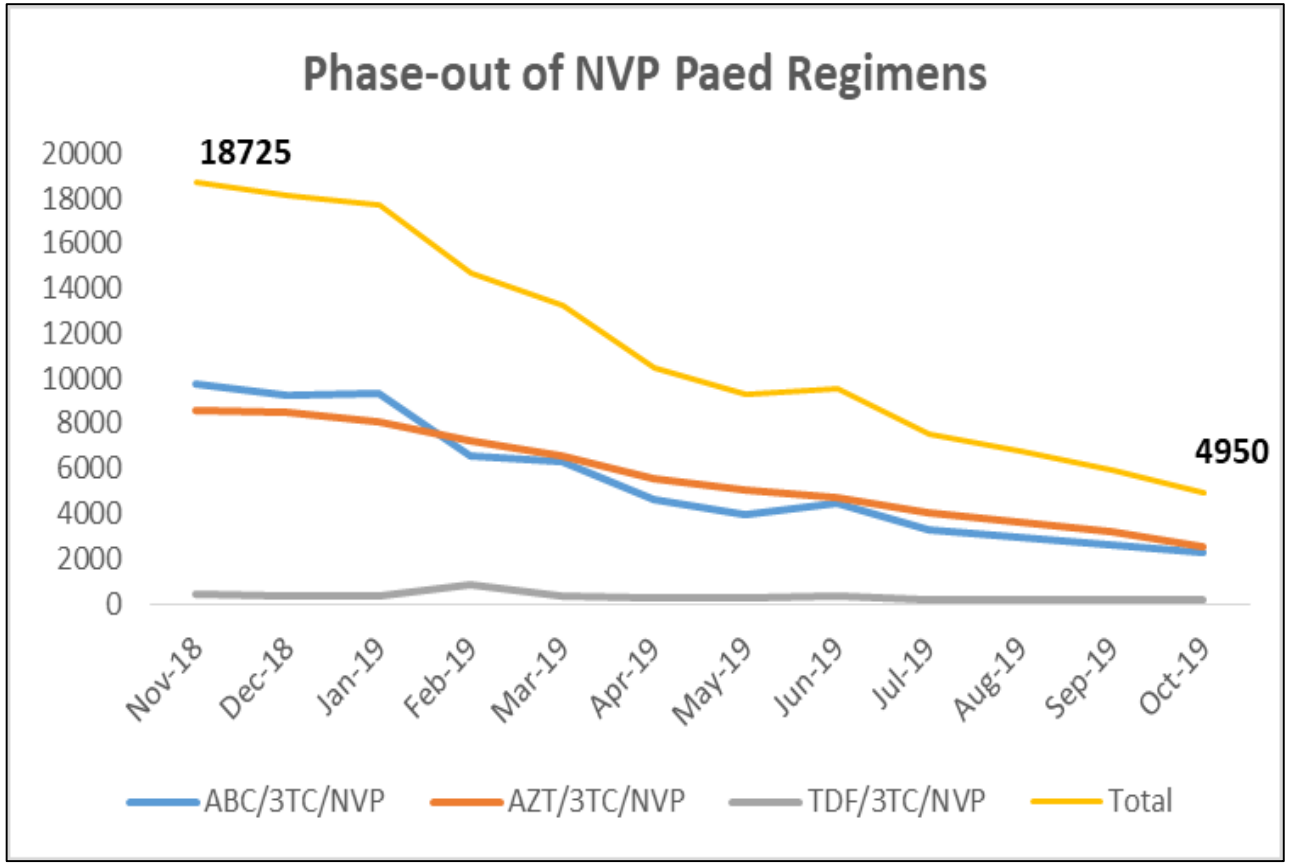
Regimen Code	ARV or OI Treatment Regimen	Number of Current Active Patients/Clients on this regimen at the end of this Reporting period
	ADULT ART	
	Adult ART 1st Line regimens	
AF1A	AZT + 3TC + NVP	10518
AF1B	AZT + 3TC + EFV	4154
AF1D	AZT + 3TC + DTG	1017
AF2A	TDF + 3TC + NVP	4910
AF2B	TDF + 3TC + EFV	413933
AF2D	TDF + 3TC + ATV/r	9122
AF2E	TDF + 3TC + DTG	438743
AF2F	TDF + 3TC + LPV/r (*1L Adults <40kg*)	1549

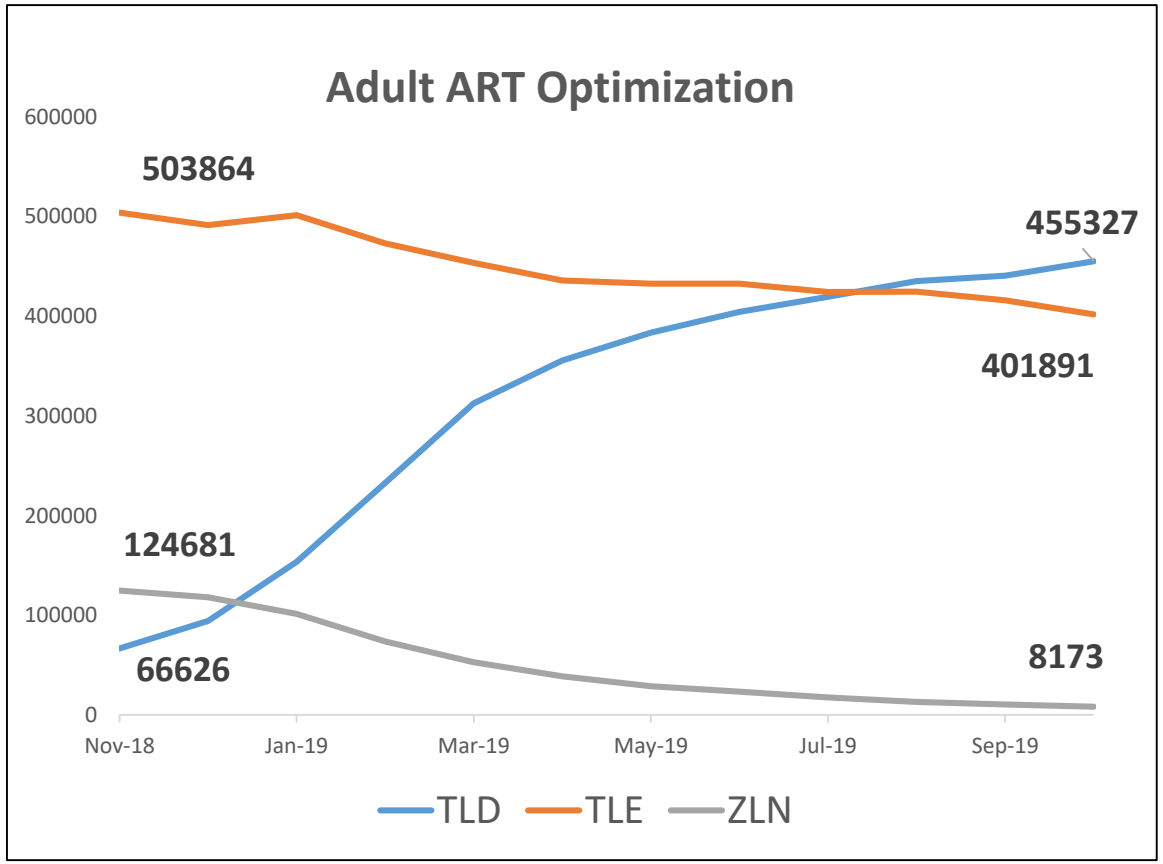
DHIS2: Pivot Tables (Adult ART Optimization)



Kenya		
Period / Data	MoH 729B Facility - F'MAPS Revision 2017 TDF + 3TC + DTG AF2E Adult ART 1st Line regimens	MoH 729B Facility - F'MAPS Revision 2017 TDF + 3TC + EFV AF2B Adult ART 1st Line regimens
November 2018	66,626	503,864
December 2018	94,266	491,304
January 2019	153,646	501,399
February 2019	232,743	473,058
March 2019	312,614	453,495
April 2019	355,729	435,915
May 2019	383,413	432,765
June 2019	404,525	432,692
July 2019	419,624	424,190
August 2019	435,119	424,637
September 2019	438,743	413,933
October 2019	451,322	437,783

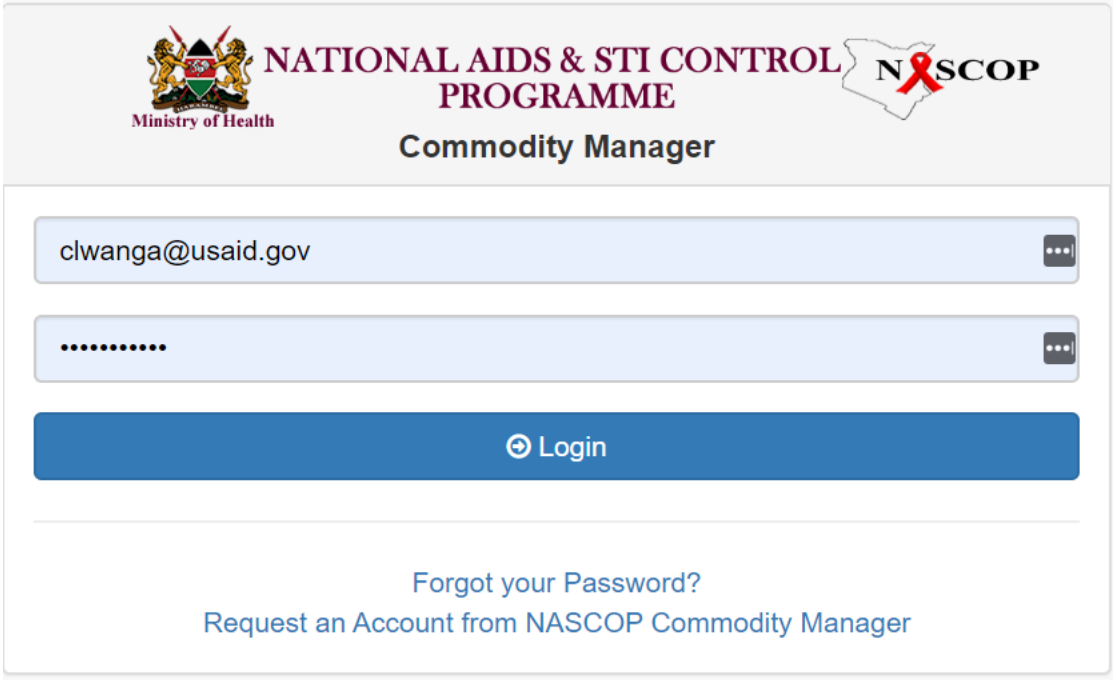
ART Optimization





Source: Kenya Health Information System (KHIS) for Aggregate Reporting

ART Commodities Manager



- Integrates downstream facility data (pulled from DHIS2) and upstream data (Pulled from the KEMSA ERP)
- Facilitates end-to-end visibility of ART supply chain data
- Key features
  - Patient statistics (Patient by regimen data)
  - Pipeline monitoring using commodity Trackers
  - Data triangulation in order management that enables matching of patient statistics and commodity data to support decision-making

Commodity Manager Dashboard

Commodity Manager

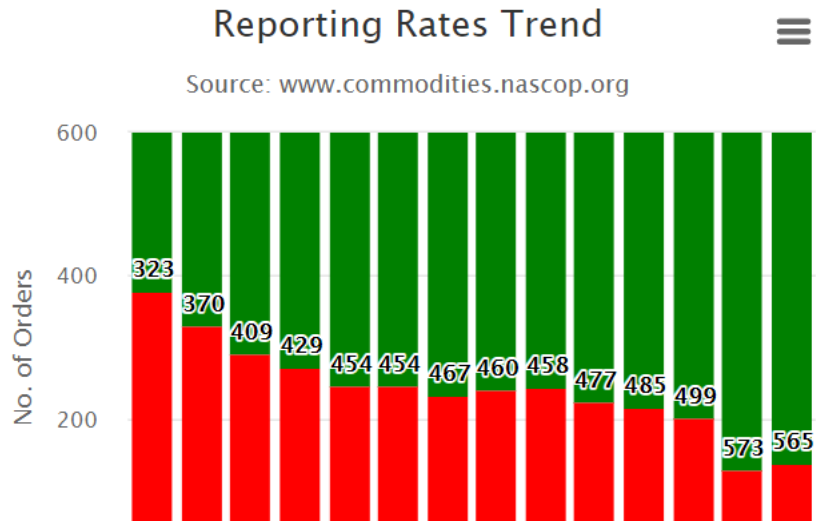
NASCOP: National | Charles Lwanga

- Main Dashboard
- Commodity Analytics
- Commodity Dashboard
- HepB
- Admin
- Orders
  - Reports
  - Reporting Rates
  - Allocation
- Procurement

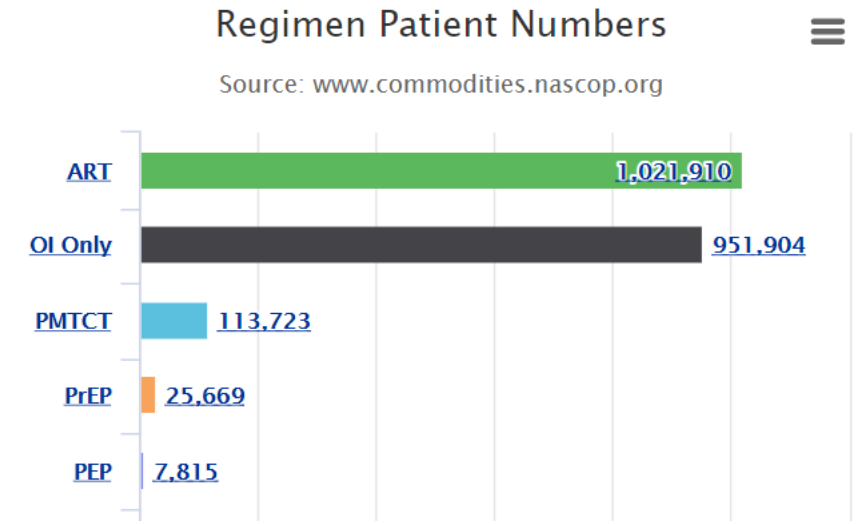
Dashboard

Advanced Filter | Year: 2015 | 2016 | 2017 | 2018 | 2019 | | Month: Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec

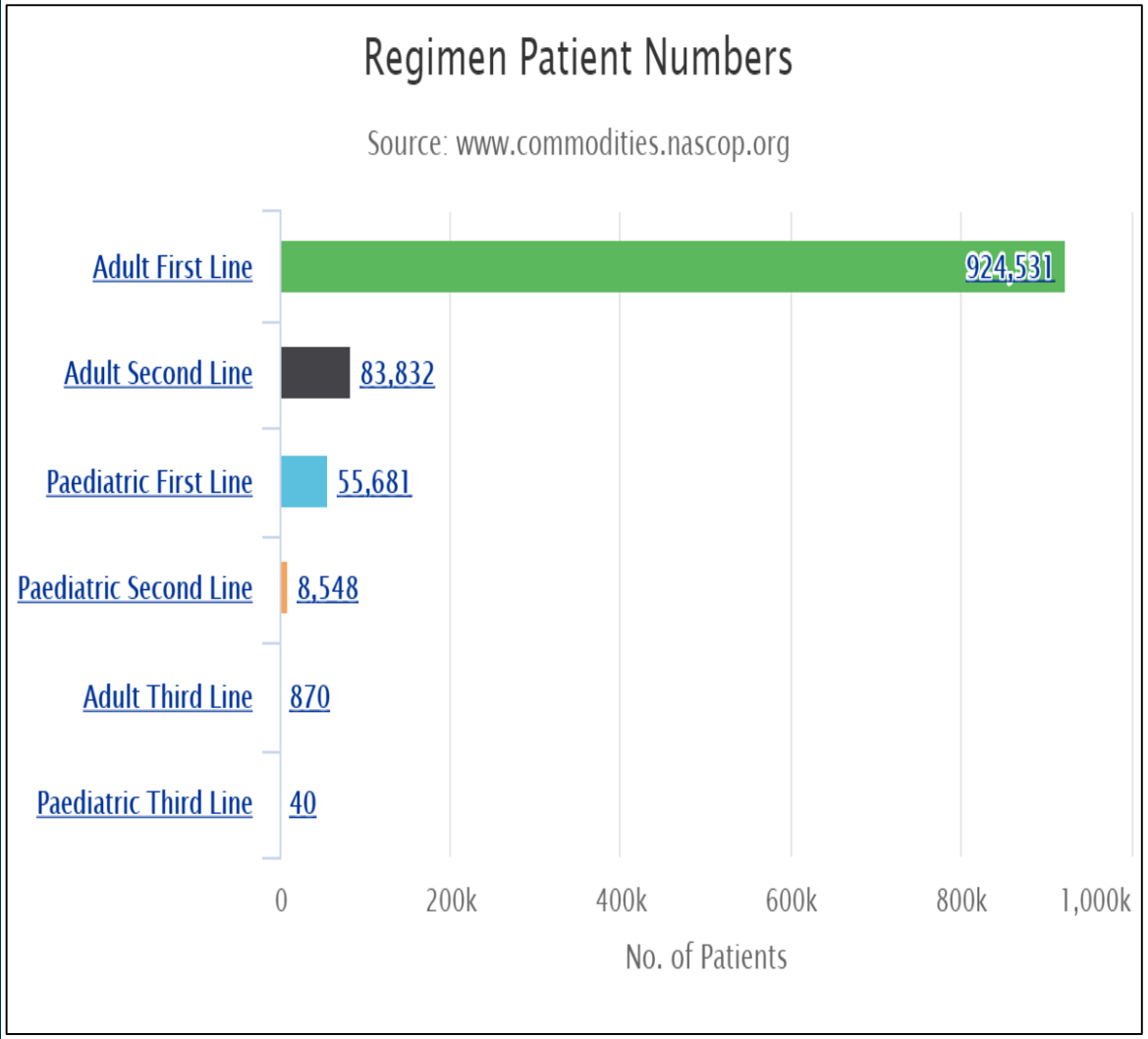
Reporting Rates

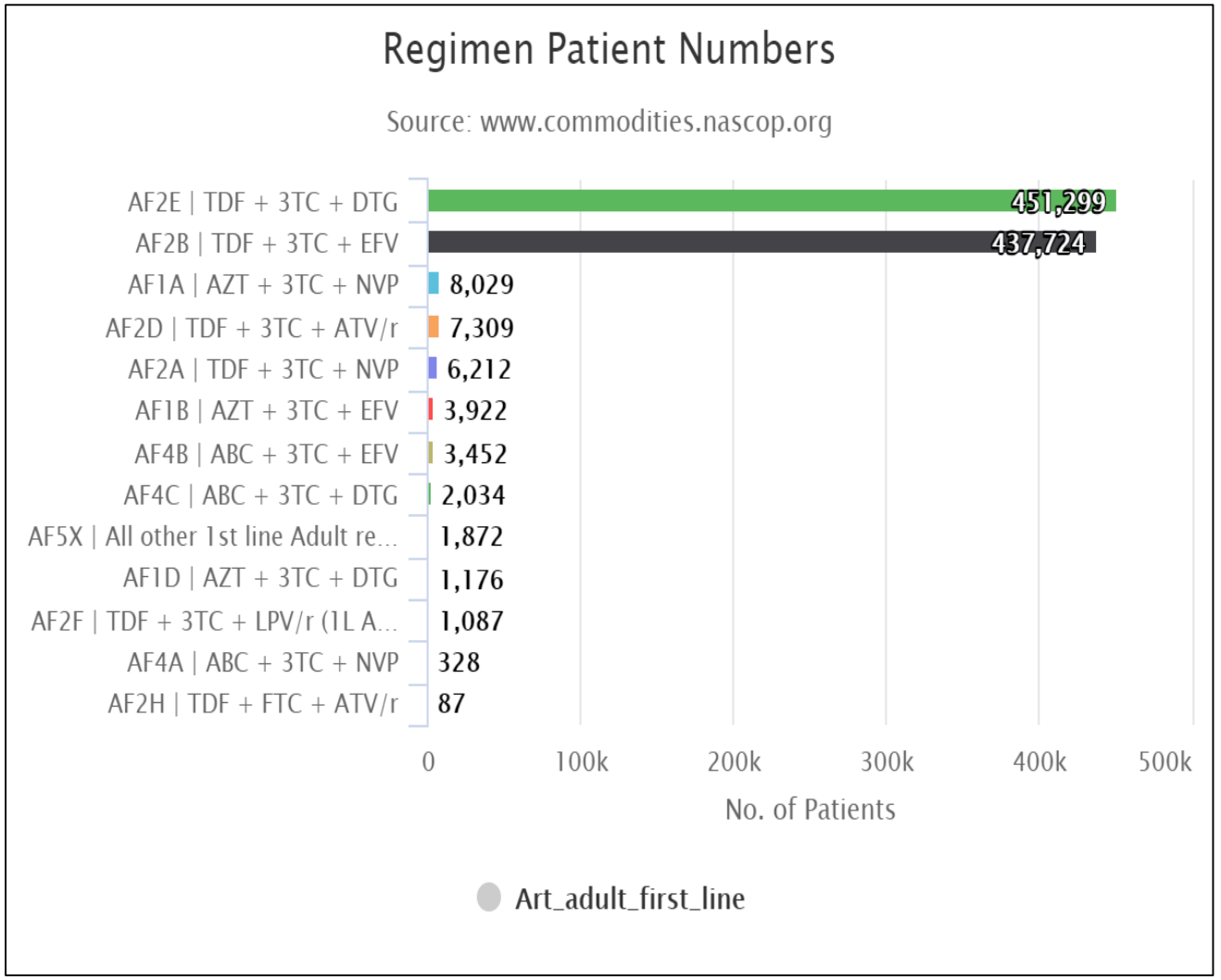


Patients by Regimen

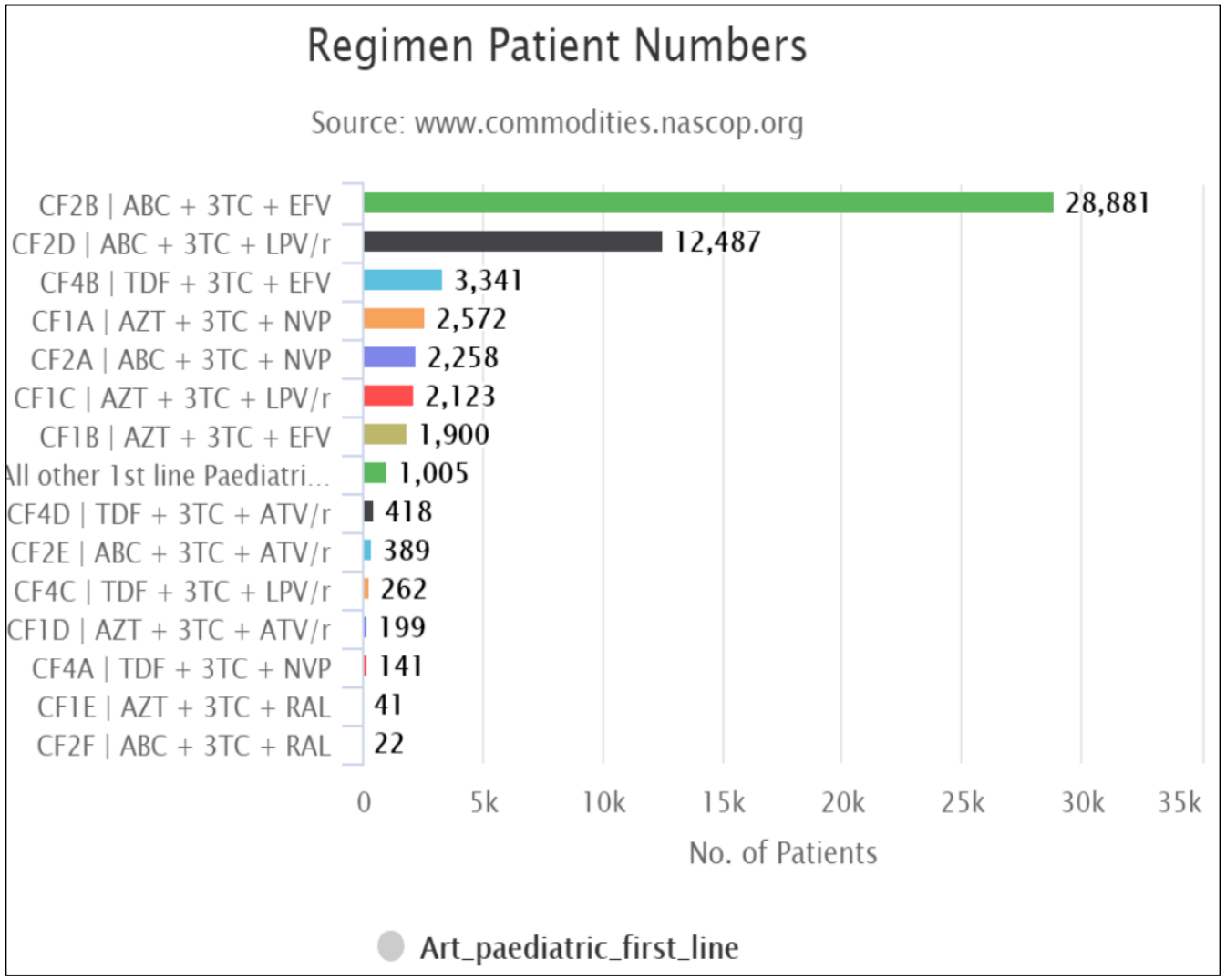


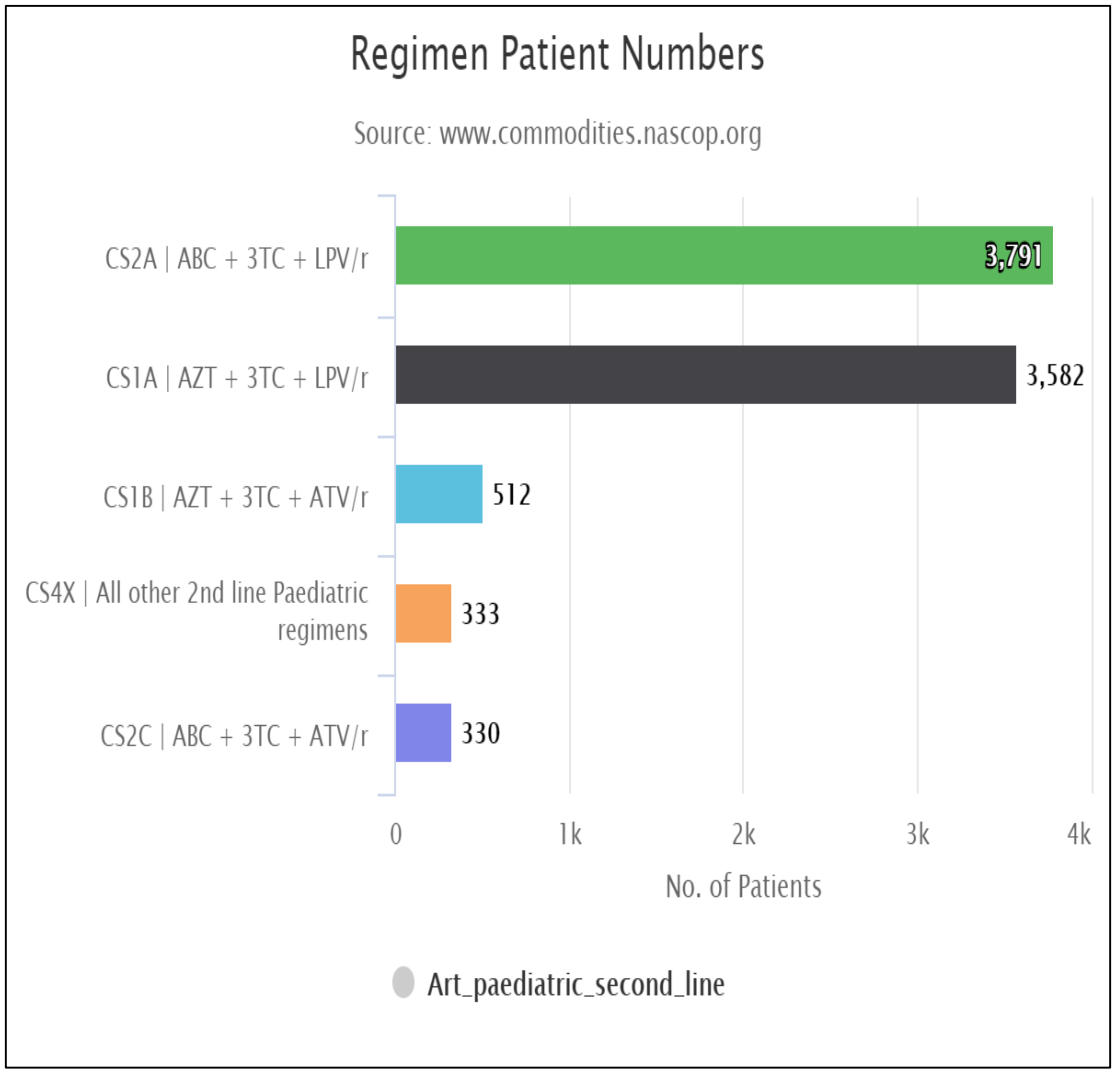
Commodity Manager: Patients by Regimen





Commodity Manager: Pediatric Patients by Regimen





Pipeline Monitoring Using the Commodity Tracker ABC/3TC 120/60MG

Abacavir/Lamivudine (ABC/3TC) 120/60mg FDC Tabs | October-2019 Tracker

Transactions

Procurement | Product Tracker | Decisions

Year: 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021

	Jan-2019	Feb-2019	Mar-2019	Apr-2019	May-2019	Jun-2019	Jul-2019	Aug-2019	Sep-2019	Oct-2019	Nov-2019	Dec-2019
Opening Balance	-	-	268,864	282,645	232,814	185,453	191,752	357,284	593,051	-	-	-
Proposed Qty.	-	-	-	-	-	-	-	-	-	-	-	-
Contracted Qty.	-	-	-	998,158	-	-	-	-	-	-	-	-
Call Down Qty.	-	-	-	-	-	-	-	-	-	-	-	-
Received Qty.	-	-	97,366	-	54,176	84,683	262,652	309,736	181,436	-	-	-
Issues to Facility	100,122	93,221	83,585	49,829	101,535	78,378	97,087	73,966	97,110	**64,238**	8,975	-
Adjustments/Losses (+/-)	-	-	-	2	2	6	-19	3	-	-	-	-
Closing Balance	-	-	282,645	232,818	185,457	191,764	357,298	593,057	677,377	**613,135**	920,732	-
Monthly Consumption	83,327	76,263	74,132	84,614	77,530	81,672	79,942	89,541	78,770	**78,573**	-	-
Average Issues	100,275	100,185	101,176	89,674	94,610	84,445	83,939	80,730	82,984	**85,386**	69,959	-
Average Consumption	77,148	76,731	77,436	78,869	77,744	79,590	79,026	81,239	82,012	**81,005**	-	-

Procurement Tracker

Atazanavir/Ritonavir (ATV/r) 300/100mg Tabs | October-2019 Tracker

Procurement | Product Tracker | Decisions

Procurement Form

Stock on Hand (SOH) 539,509

Months of Stock (MOS) 5.3

System Calculated Order Quantity 992,456

Procurement Quantities

drug_id	year	month	proposed	contracted	calldown	received	comments	funding_agents	suppliers
8	2019	Jan	0	0	0	0			
8	2019	Feb	0	0	0	0			
8	2019	Mar	0	0	0	0			
8	2019	Apr	0	0	0	108			
8	2019	May	0	0	0	227420			

Parameters

- SOH data (Packs)
- SOH (MOS)
- Proposed Quantities
- Contracted
- Call down Quantities
- Quantities Received
- Funding agent
- Supplier details
- System calculated Order Quantities

Commodity Manager: Decisions Tracker

Tenofovir/Lamivudine (TDF/3TC) 300/300mg FDC Tabs | October-2019 Tracker

Procurement | Product Tracker | Decisions

Decisions

DISCUSSIONS	RECCOMMENDATIONS
14 Nov/19	
At 4 MOS. Pending USAID: 229,144 delivery expected by mid-Oct 2019 Pending GF:- 148,650 already in sea	KEMSA to follow up with expected supplies for clearance and distribution.
11 Oct/19	
At 4.7 MOS. Pending USAID: 229,144 delivery expected by mid-Oct 2019 Pending GF:- 129,382 in country awaiting clearance, 148,650 ready for dispatch in Dec 2019	KEMSA to follow up with expected supplies for clearance and distribution.
13 Sep/19	
At 5.5 MOS. Pending USAID: 229,144 Pending GF: 680,473- 129,382 in country awaiting clearance 48,650 ready for dispatch in Dec 2019	KEMSA to follow up with expected supplies for clearance and distribution.
16 Aug/19	
At 3 MOS. 115,856 re 6th August USAID: 200,000: 170,859 in country- under clearance, 29,144 awaiting shiping documents.Balance is 200,000. GF: 796,319 packs: 115,849 received,129,382 expected by 26th August 2019,pending balances of 200,000.	KEMSA to follow up with expected supplies for clearance and distribution.

Commodity Manager: Order Management (1)

Copy | CSV | Excel | PDF | Print

Drug Name	End Month Stock on Hand	Days out of Stock	Resupply Quantity	AMC	Facility MOS	AutoCalc Resupply	Allocated	Allocated MOS
	L	Expiry Date	M	N		P	Q	O R	S
Tenofovir/Emtricitabine 300/200mg FDC	26		0	3	8.67	0		
Tenofovir/Lamivudine 300/300mg FDC	160		30	39	4.10	0	30	1
Tenofovir/Lamivudine (TDF/3TC/EFV) 300/3 FDC Tabs			0	0	0.00	0		
Tenofovir/Lamivudine (TDF/3TC/EFV) 300/3 FDC Tabs	1434		0	694	2.07	648		

Copy | CSV | Excel | PDF | Print

	Code | Regimen	No. of Patients
ADULT FIRST LINE		
⊕	AF1A | AZT + 3TC + NVP	10
⊕	AF1B | AZT + 3TC + EFV	12
⊕	AF2B | TDF + 3TC + EFV	562
⊕	AF4B | ABC + 3TC + EFV	1
⊕	AF1D | AZT + 3TC + DTG	4
⊕	AF2E | TDF + 3TC + DTG	380

Commodity Manager: Order Management (2)

Copy | CSV | Excel | PDF | Print

Drug Name	End Month Stock on Hand	AMC	AutoCalc Resupply	Allocated	Allocated MOS	Comments	Decision
	N		P	Q O	R	S	T	U
Tenofovir/Emtricitabine 300/200mg FDC	26	3	0				REDISTRIBUTE
Tenofovir/Lamivudine 300/300mg FDC	160	39	0	30	1		MONITOR
Tenofovir/Lamivudine (TDF/3TC/EFV) 300/3 FDC Tabs		0	0				RESUPPLY
Tenofovir/Lamivudine (TDF/3TC/EFV) 300/3 FDC Tabs	1434	694	648				RESUPPLY

Copy | CSV | Excel | PDF | Print

	Code | Regimen	No. of Patients
ADULT FIRST LINE		
⊕	AF1A | AZT + 3TC + NVP	10
⊕	AF1B | AZT + 3TC + EFV	12
⊕	AF2B | TDF + 3TC + EFV	562
⊕	AF4B | ABC + 3TC + EFV	1
⊕	AF1D | AZT + 3TC + DTG	4
⊕	AF2E | TDF + 3TC + DTG	380

Commodity Manager: Communication

Ministry of Health, NASCOP Unit

Kenya Anti-Retroviral medicines (ARVs) Stock Situation –Sept 2019 Final

Key Highlights:

A. Number of Patients on ART

As at end Sept 2019: ---------- 1,115,674

Adult patients ---------- 1,051,901

Paediatric patients---------- 63,773

**NB: Reporting rate is 88.8% for patients' numbers in DHIS2; Excludes private sector data.*

B. Supporting agencies of above patients

- GoK
- GF
- USG

C. Average scale-up rate (12 months rolling) for ART: 5,525 patients per month

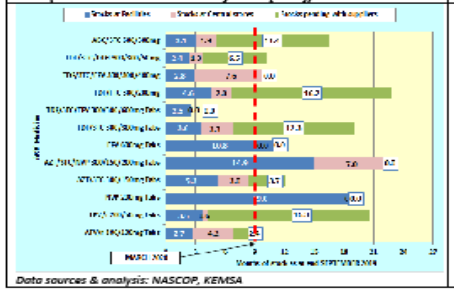
- Adults: 5,969 patients per month
- Children: -443 patients per month

Key regimens in use	No. of patients on ART *2nd line, other codes listed as per ART LMIS tools*	
Adults	**Patient numbers**	**% proportions**
TDF+3TC+DTG	436,002	40.4%
Regimen 1: TDF+3TC+EFV	481,049	44.5%
Regimen 2: TDF+3TC+NVP	5,363	0.5%
Regimen 3: AZT+3TC+NVP	11,333	1.0%
Regimen 4: AZT+3TC+EFV	4,638	0.4%
2nd Line: LPV/r-based regimens	18,967	1.8%
2nd Line: ATV/r-based regimens	72,223	6.7%
PreP	28,246	2.6%
Other regimens	22,326	2.1%
Children	**Patient numbers**	**% proportions**
Regimen 1: ABC+3TC+NVP	2,554	4.0%
Regimen 2: ABC+3TC+EFV	27,493	43.1%
Regimen 3: AZT+3TC+NVP	3,142	4.9%
Regimen 4: AZT+3TC+EFV	1,897	3.0%
Regimen 5: ABC+3TC+LPV/r (1st line)	12,060	18.9%
Regimen 6: AZT+3TC+LPV/r (1st line)	2,184	3.4%
2nd Line: LPV/r-based regimens	7,267	11.4%
2nd Line: ATV/r-based regimens	834	1.3%
Other regimens	6,342	9.9%

3TC = Lamivudine; ABC = Abacavir; ATVir = Atazanavir with Ritonavir; AZT = Zidovudine; ART = Antiretroviral Therapy; EFV = Efavirenz; FDC = Fixed Dose Combination; GF = Global Fund; GoK = Government of Kenya; KEMSA = Kenya Medical Supplies Authority; KP = Kenya Pharma; LPVir = Lopinavir with Ritonavir; NASCOP = National AIDS & STI Control program; NVP = Nevirapine; OIs = Opportunistic infections; Paed = Paediatric; TDF = Tenofovir; USG = United States government.

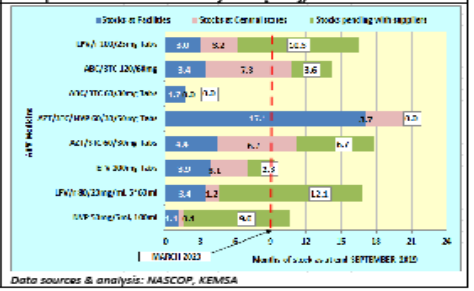
National ARV Stock Status (Adult and Paediatric)

Figure 1: Adult ARV Stock status at KEMSA as at end September 2019 (based on Patient months-of-stock [MoS])



Data sources & analysis: NASCOP, KEMSA

Figure 2: Paediatric ARV Stock status at KEMSA as at end September 2019 (based on Patient months-of-stock [MoS])



Data sources & analysis: NASCOP, KEMSA

Elements: Monthly ARV Stock Situation Report "2 Pager Report"

- Total number of patients on treatment
- Scale-up Numbers
- Patients by Regimen (# & %)
- SOH at Facility level (MOS)
- SOH at KEMSA (MOS)
- Quantities on order (MOS)
- Red-flag items

United Republic of Tanzania

Supply Chain Optimization and Country Uptake

4th ARV Buyer Supplier Summit

Mercy Mpatwa

27th November, 2019

Background Information

- Population : 55,890,747
- Prevalence : 4.7%
- Estimated PLWHIV 1.6 M

- 1,252,205 of PLWHIV know their status (78.3%)

- 1,221,799 of PLWHIV are on ART (97.6)

Scope of Demand Forecast

- 2-year Forecast
  - Jan 2020 to Dec 2021

- 2-year Supply plan
  - Jan 2020 to Dec 2021

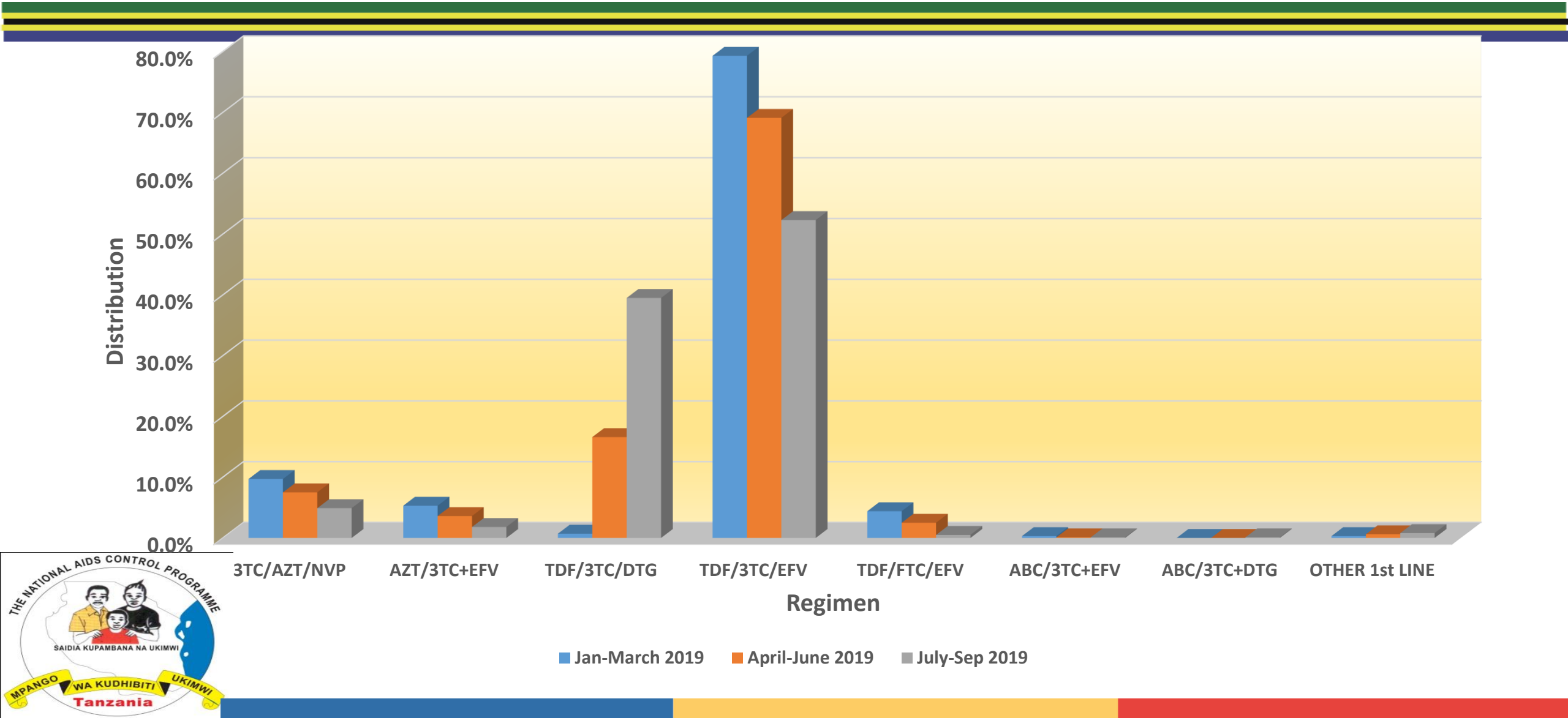
- Forecast scenario

  Test and Treat All new Targets with adult 1st line ART clients transition to TLD and Pediatric ART clients transition to DTG and LPV/r based ARV regimens based on the revised Guideline for management of HIV and AIDS 2019

Sources of Data

- Epicor 9 – Stock Status at Central level (MSD)
- CTC2 Database – ART clients distribution by regimen (Health Facilities)
- e-LMIS – consumption data and trends (Health Facilities)

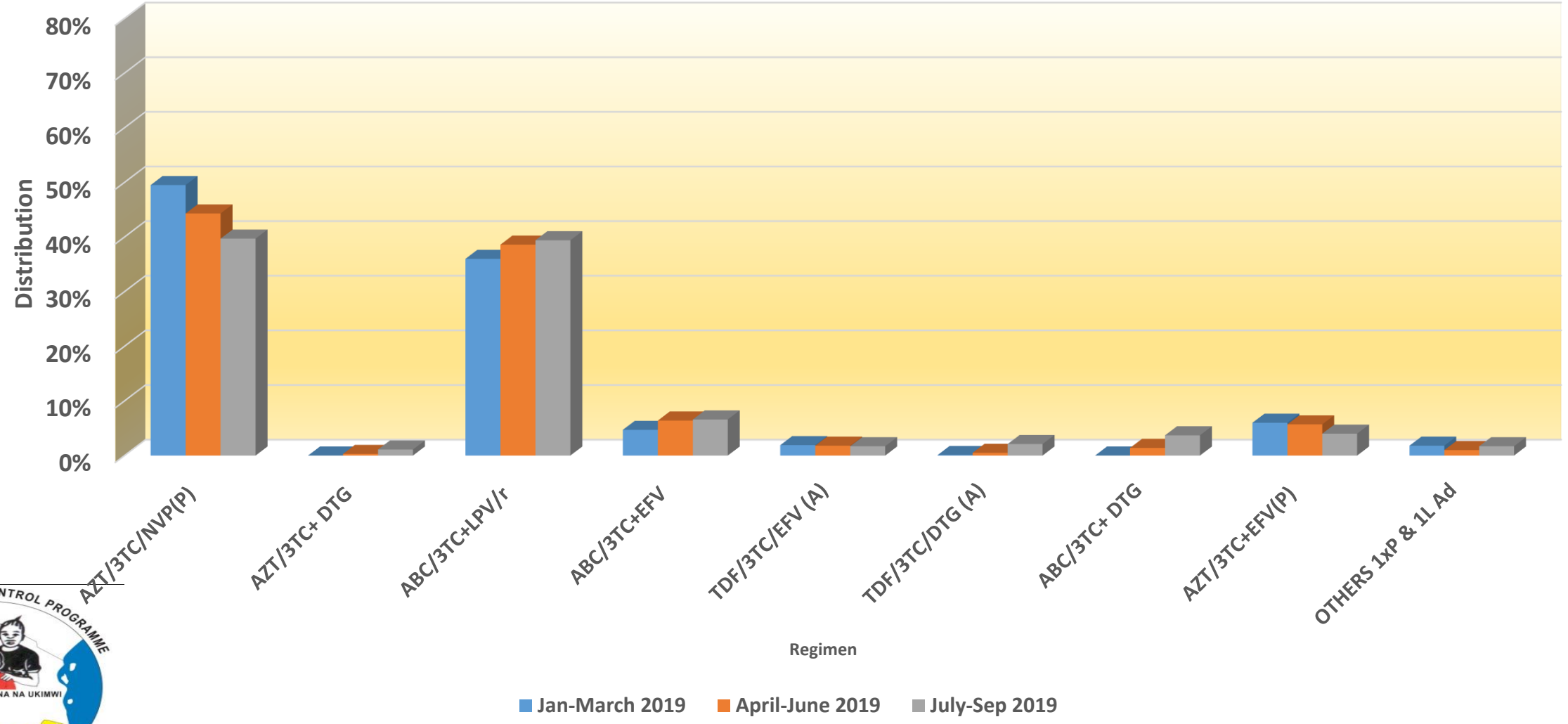
1st Line Adult Regimens – CTC2 data



Adults first line ARV regimens (existing clients)

First Line Regimens	Actual % distribution Oct-Dec 2018	Actual % distribution July-Sept 2019	Jul 2019- June 2020	Jul 2020 – June 2021	Jul 2021 –June 2022
TDF/3TC/DTG	0.0%	39.5%	54.0%	85%	85.0%
TDF /3TC/EFV	77.0%	52.3%	30.0%	10.0%	10.0%
AZT/3TC + EFV	6.1%	1.8%	5.8%	0.0%	0.0%
ABC/3TC+EFV	0.2%	0.1%	0.2%	0.0%	0.0%
AZT/3TC/NVP	12.1%	4.9%	8.0%	0.0%	0.0%
TDF/FTC/EFV	4.1%	0.5%	0%	0.0%	0.0%
ABC/3TC+DTG	0.0%	0.1%	2%	5.0%	5.0%

1st Line Pediatric Regimens – CTC2 data



Progress to date

- Multi Month Dispensing
- Redesigned Logistics System
- Bottom Up Quantification
- Data visibility –Web based
- Logistics Management Services
- IMPACT Team Approach
- Supply chain stakeholders engagement (e.g GHSC- TA)

Challenges

- Expiries
  - Transitions
- Stock out for optimized ART regimens delayed transition to Optimized ART;
- Compliance to TMDA requirements

Thank you for listening

Asante sana!

Supply Chain Optimization
GHSC-PSM Experience

USAID GLOBAL HEALTH SUPPLY CHAIN PROGRAM

Procurement and Supply Management

USAID
FROM THE AMERICAN PEOPLE

PEPFAR
U.S. President's Emergency Plan for AIDS Relief

*We must ensure that **the right commodities, reach the right people, in the right places, and at the right time.***

Amb. Birx

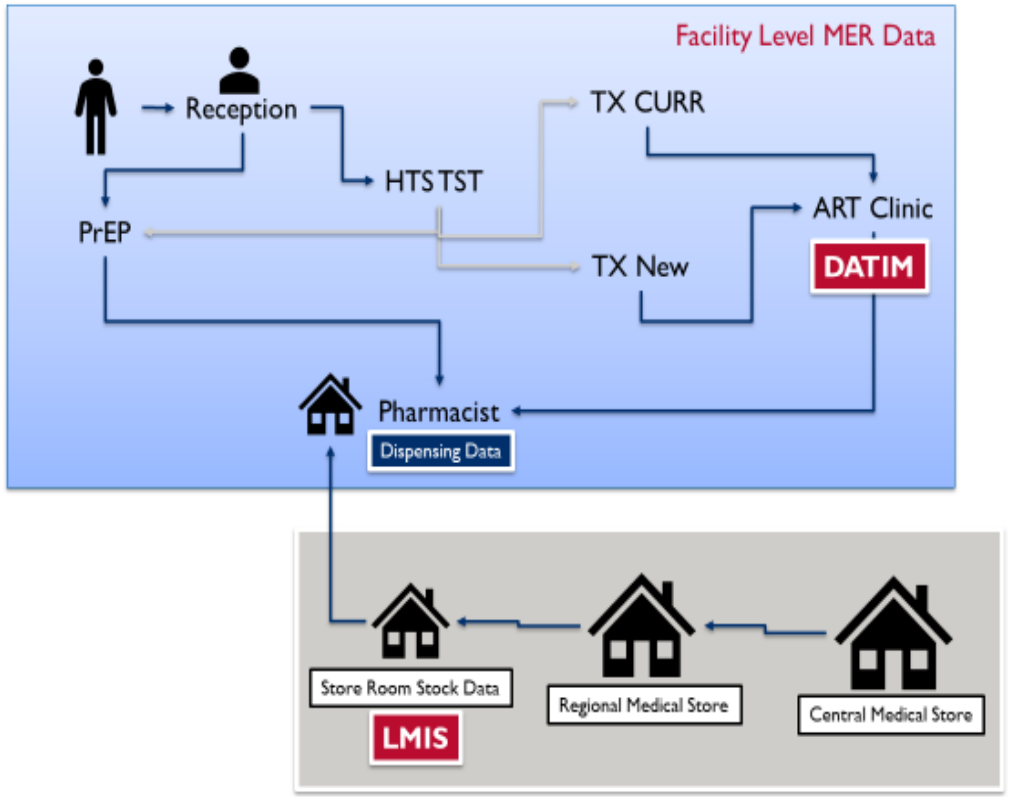
May 17, 2018

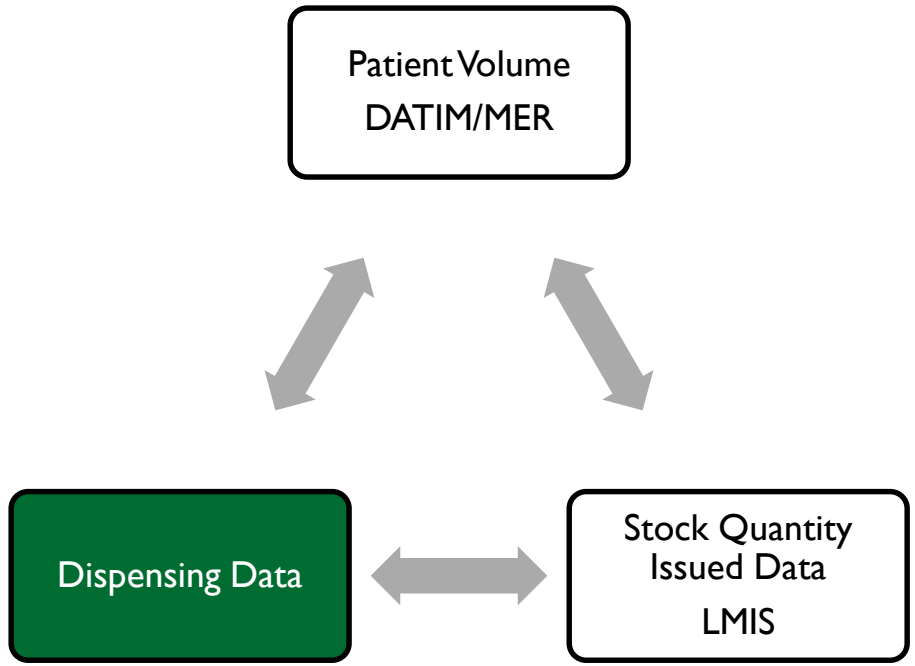
USAID
FROM THE AMERICAN PEOPLE

PEPFAR
U.S. President's Emergency Plan for AIDS Relief

Vision

Validate that every person accessing HIV/AIDS services leaves a health facility with the prescribed quantity of HIV medicine, a planned procedure or other services that they need.



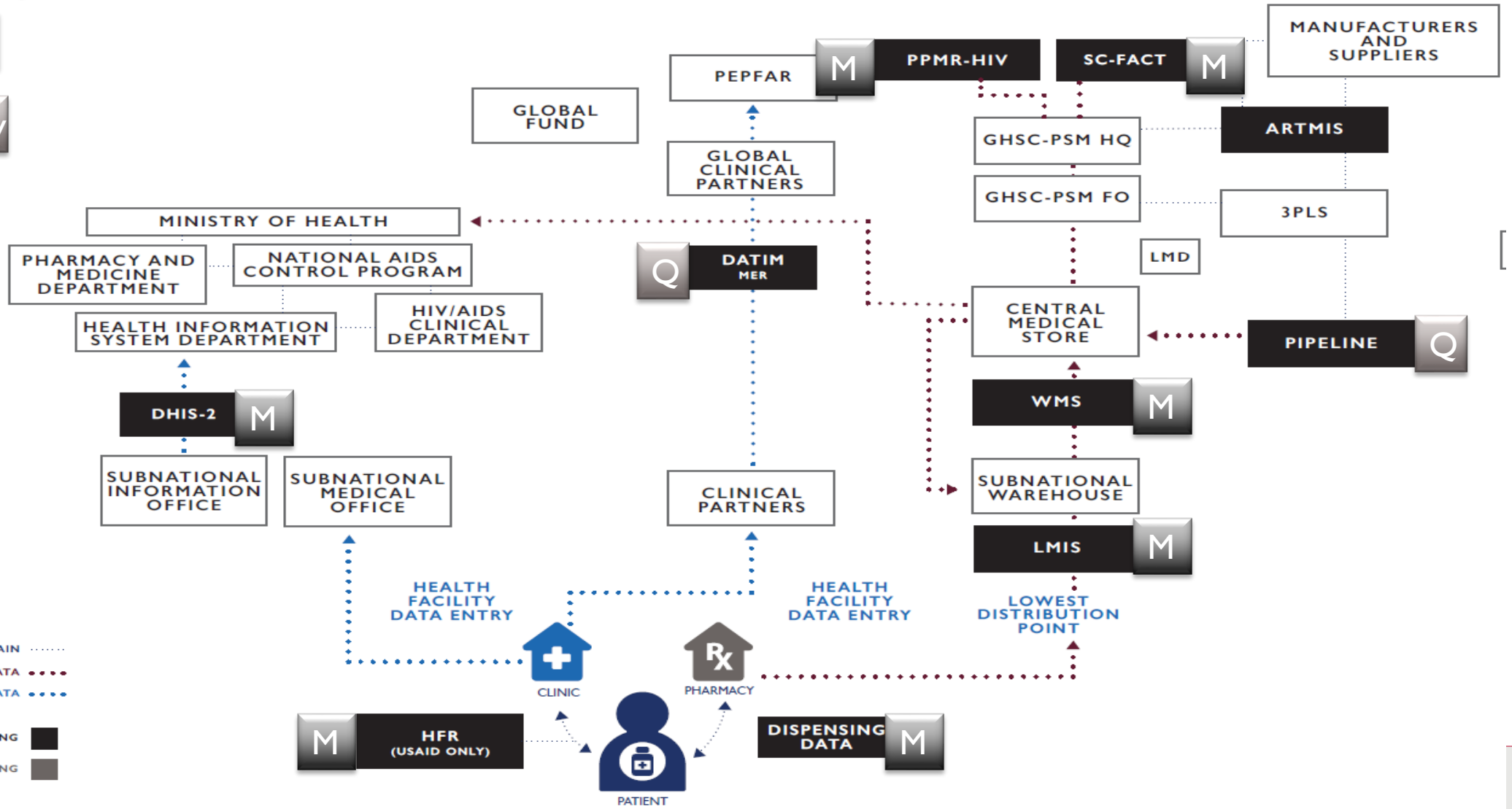


USAID GLOBAL HEALTH SUPPLY CHAIN PROGRAM
Procurement and Supply Management

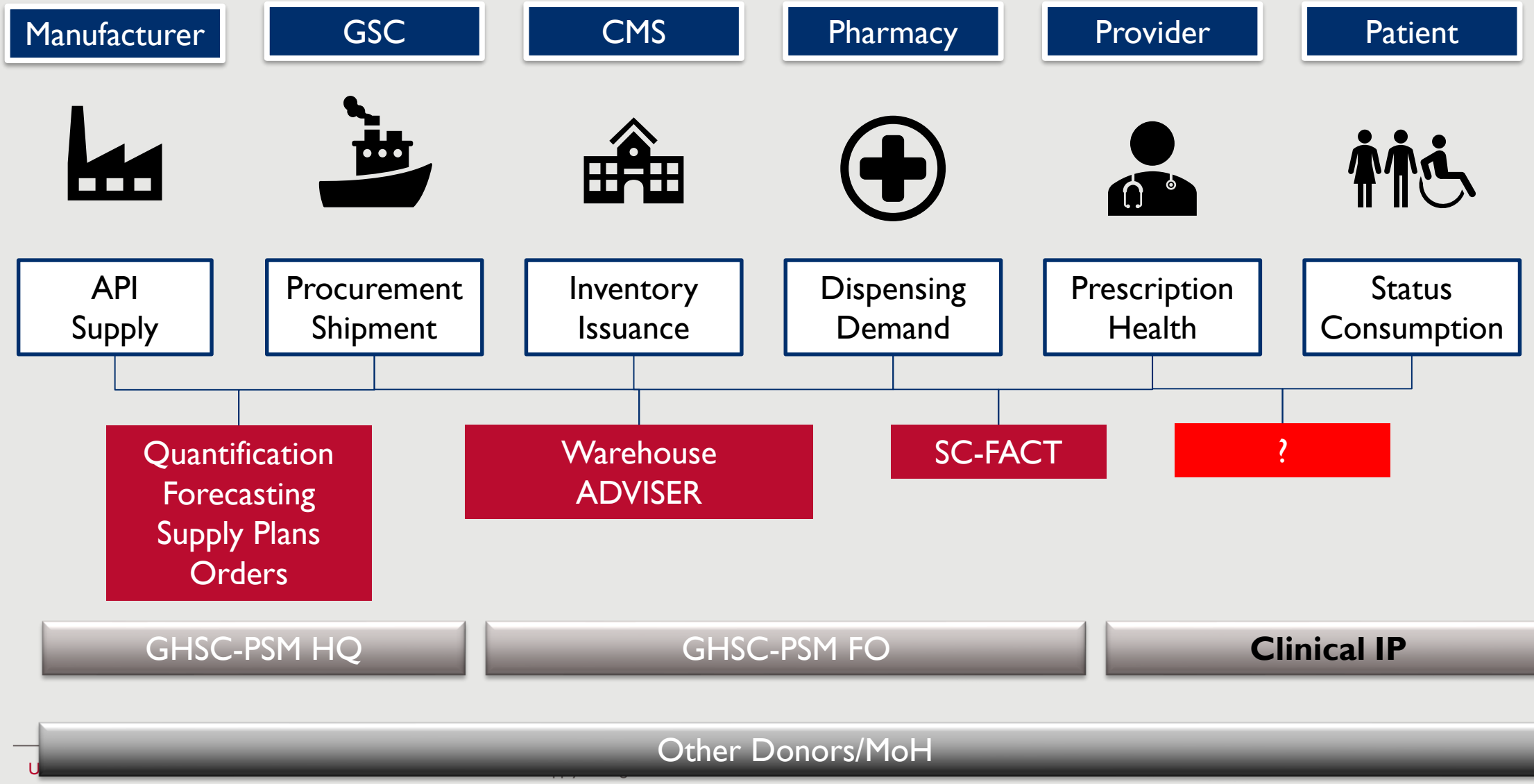
ALL AVAILABLE DATA SYSTEMS FOR HIV/AIDS PATIENT DATA TRIANGULATION

M - Monthly

Q - Quarterly



Supply Chain Stakeholder, Insights, Tools, and Data Providers



GHSC-PSM TO1-funded Supply Chain Systems Strengthening, Procurement, and Last-Mile Delivery in FY 2019

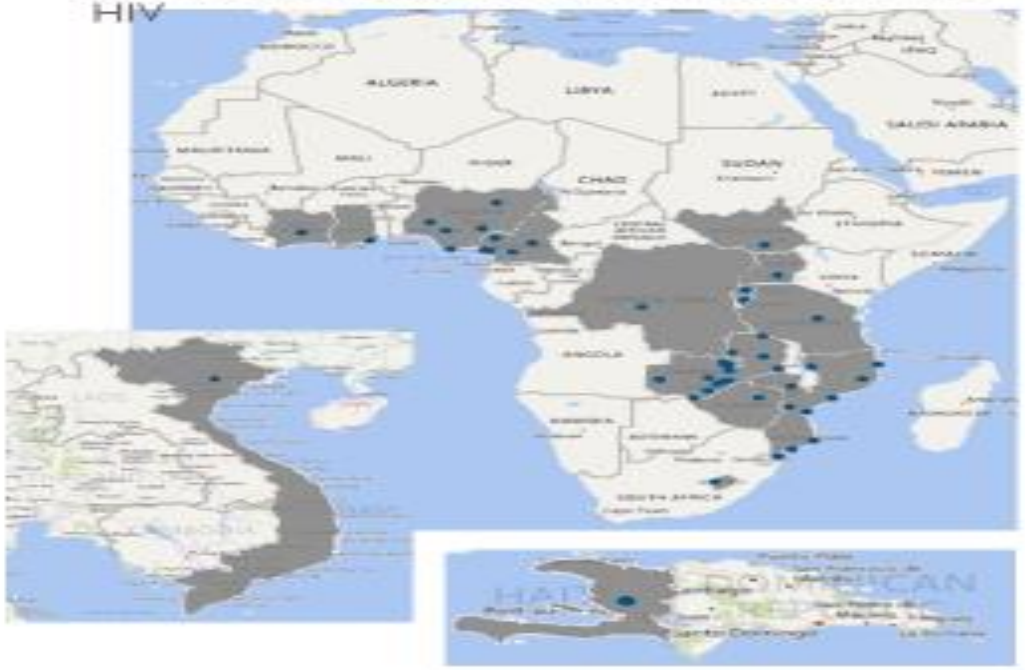
AFRICA				AFRICA (cont.)				AFRICA (cont.)			
	TA	PROC	LMD		TA	PROC	LMD		TA	PROC	LMD
Angola	■	■		Mali	■	■		Zimbabwe	■	■	■
Botswana	■	■		Mozambique	■	■					
Burkina Faso		■		Namibia	■	■		**ASIA**			
Burundi	■	■		Niger		■		Burma	■	■	
Cameroon	■	■		Nigeria	■	■	•	Cambodia	■		
Côte d'Ivoire		■		Rwanda	■	■		Indonesia	■		
DRC		■		Senegal		■		Papua New Guinea		■	
Eswatini	■	■		**South Africa**		■		Vietnam	■	■	
Ethiopia	■	■		South Sudan	■	■		**LAC**			
Ghana	■	■	•	**Tanzania**		■		Haiti	■	■	■
Kenya	■			Togo		■					
Lesotho	■			Uganda	■	■					
Malawi	■	■		Zambia	■	■	■				

TA = technical assistance; Proc = procurement; LMD = last mile distribution of commodities by GHSC-PSM.
Note: GHSC-PSM delivers to some but not all facilities in countries with •.

HIV/AIDS Supply Chain - Last Mile Data Visibility

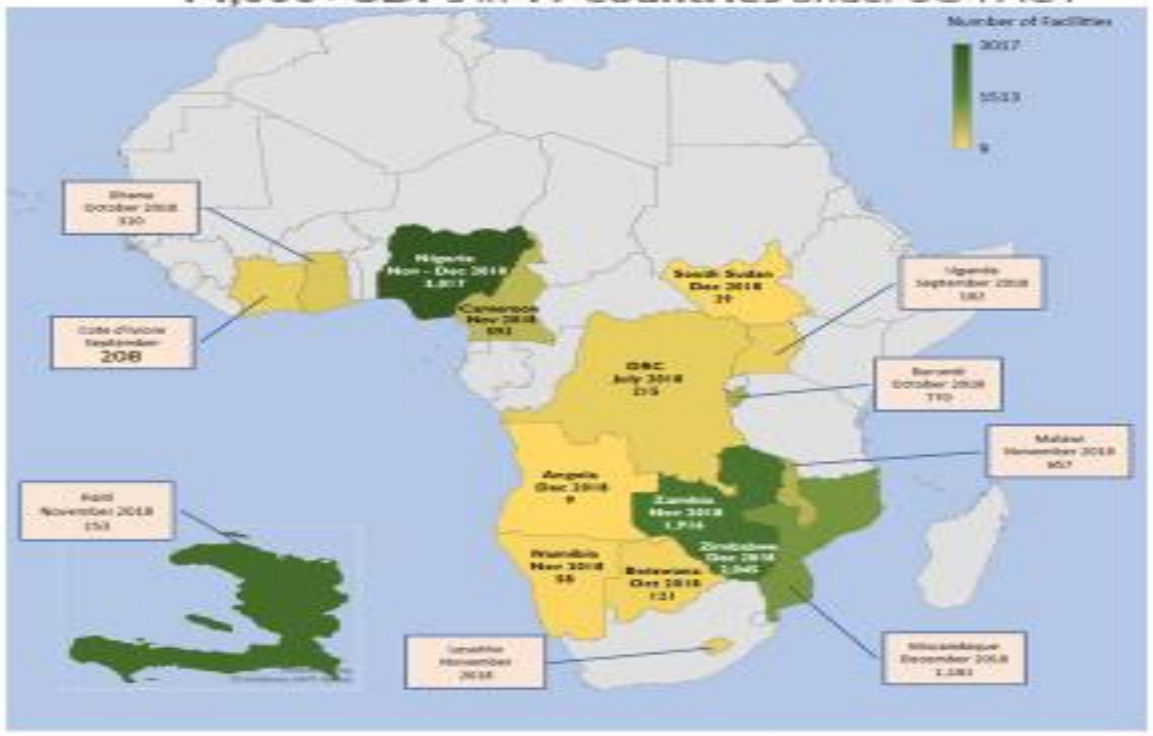
GHSC PSM Monthly Central Warehouse Inventory data Reporting Countries

59 Warehouses in 16 countries under PPMR-HIV



GHSC PSM Monthly Site-level Inventory data Reporting Countries

14,000+ SDPs in 17 countries under SC-FACT



- As of today, we have monthly 14,000 sites and 59 warehouses
- **Access to MER/Patient Data -** Piloting Integration of Data Collections

Warehouse ADVISER
AIDS Data VISibility, Evaluation and Reporting

ARVs –
Adult, Pediatric
RTKs
IPT

More than **20 HIV/AIDS Commodities** monitored at **63 warehouses** under Warehouse ADVISER **in 18 countries** since May 2018

Warehouse ADVISER Reporting Countries

18 +2

Reporting countries
Botswana, Burundi, Cameroon, Cote d'Ivoire, DRC, eSwatini, Ethiopia, Ghana, Haiti, Lesotho, Mozambique, Namibia, Nigeria, Rwanda, Uganda, Vietnam, Zambia, Zimbabwe. Malawi and South Sudan only provide data for the OGAC FLARE report.

32

Field office staff spend on average 6 hours on data entry and providing written context to clarify in-country stock level data per month.

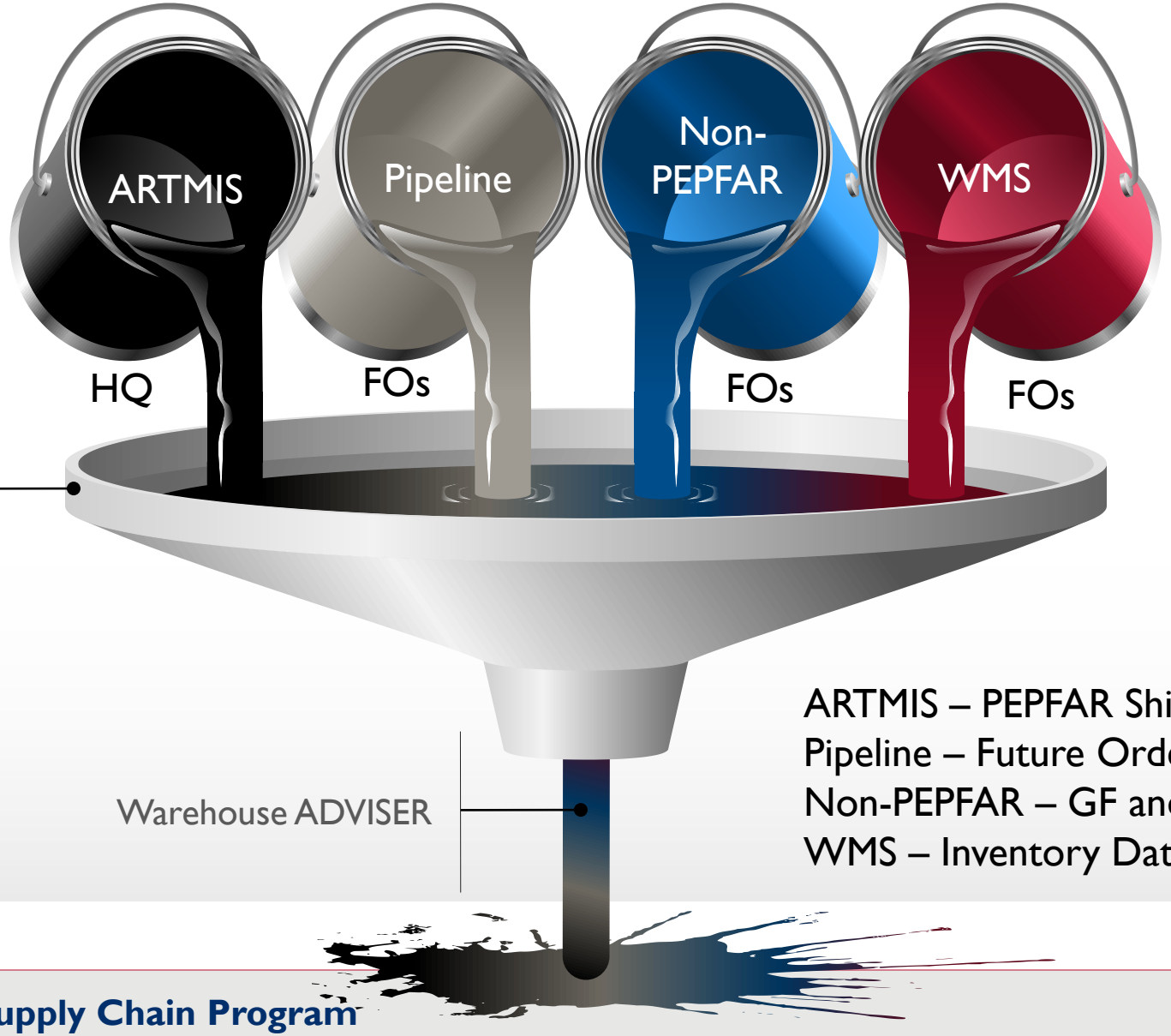
23

Products on average are reported per country, which is 365 products lines that are reported and reviewed every month (assuming all countries report monthly).

348

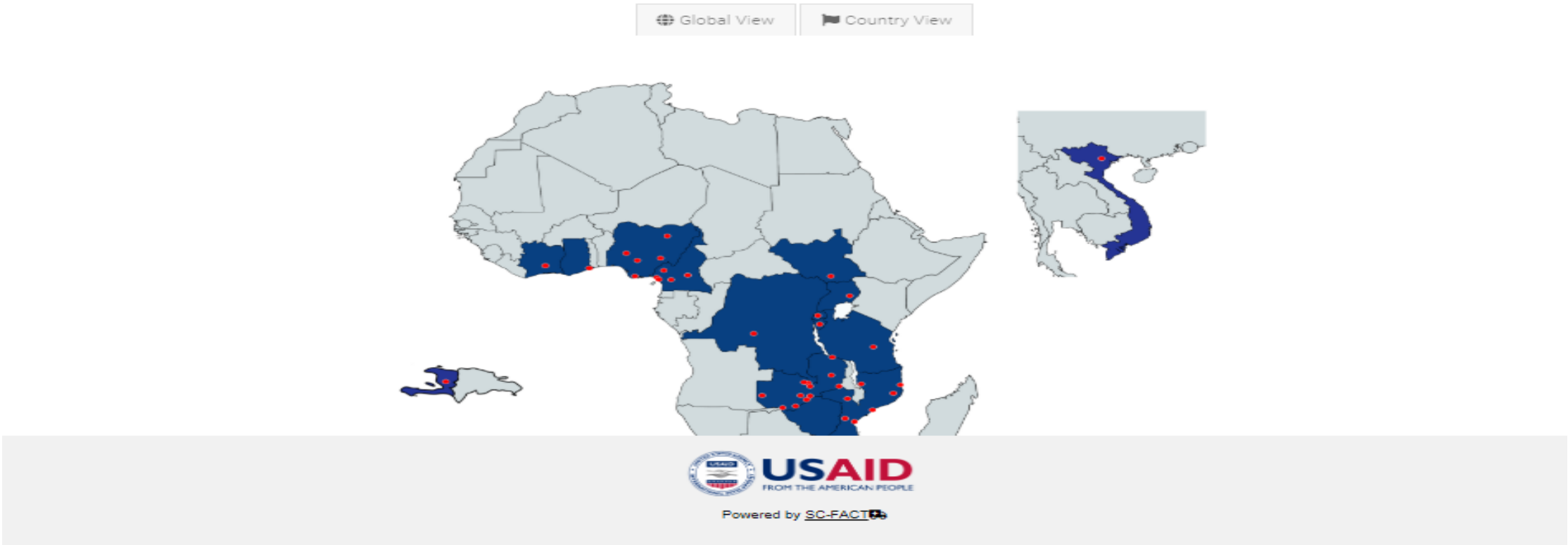
GHSC-PSM orders reviewed on a monthly basis.

Multiple Data sources are captured/merged to develop **Warehouse ADVISER**

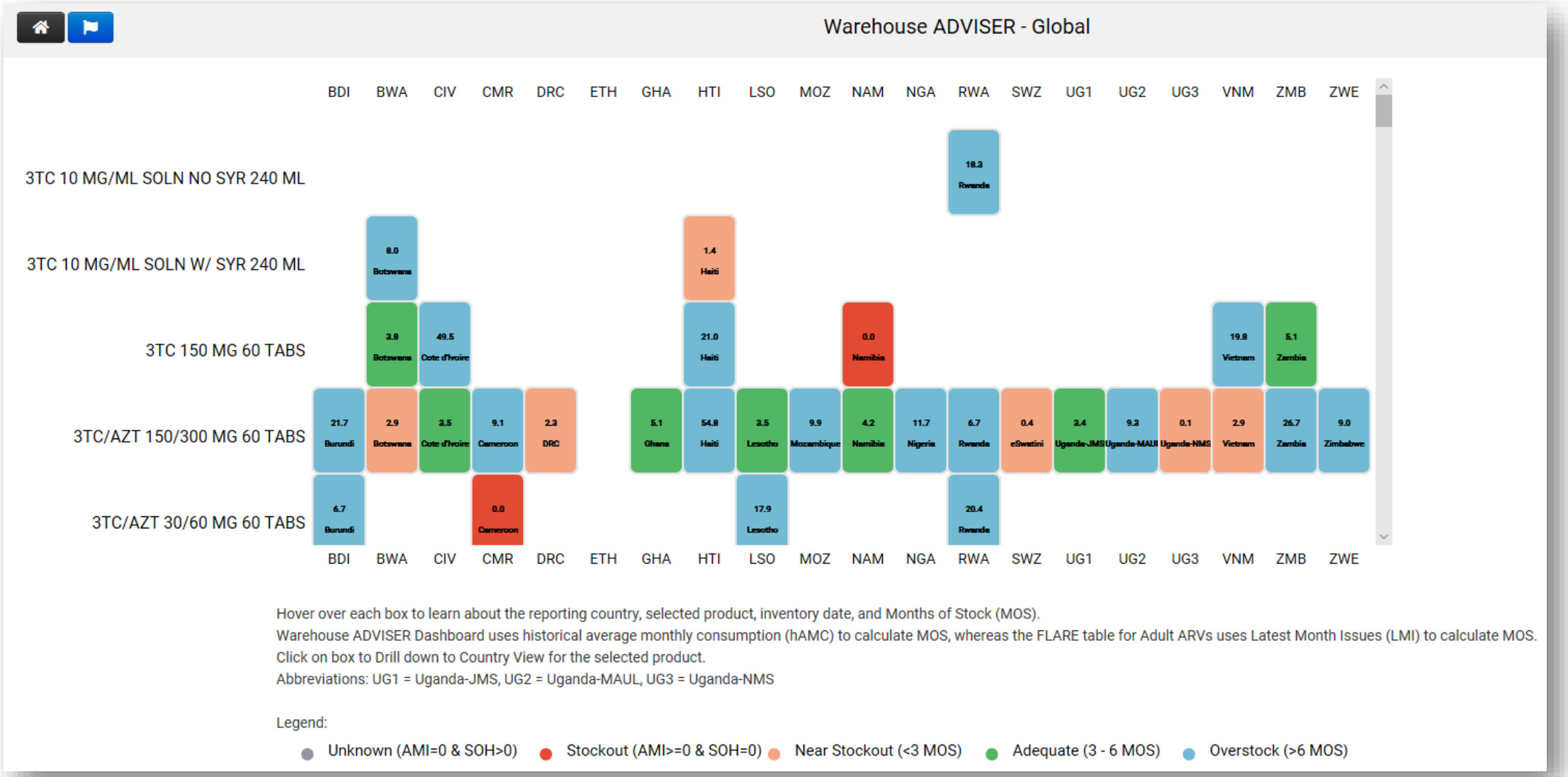


ARTMIS – PEPFAR Shipments
Pipeline – Future Orders
Non-PEPFAR – GF and MOH Orders
WMS – Inventory Data from Warehouses

Warehouse ADVISER Tool



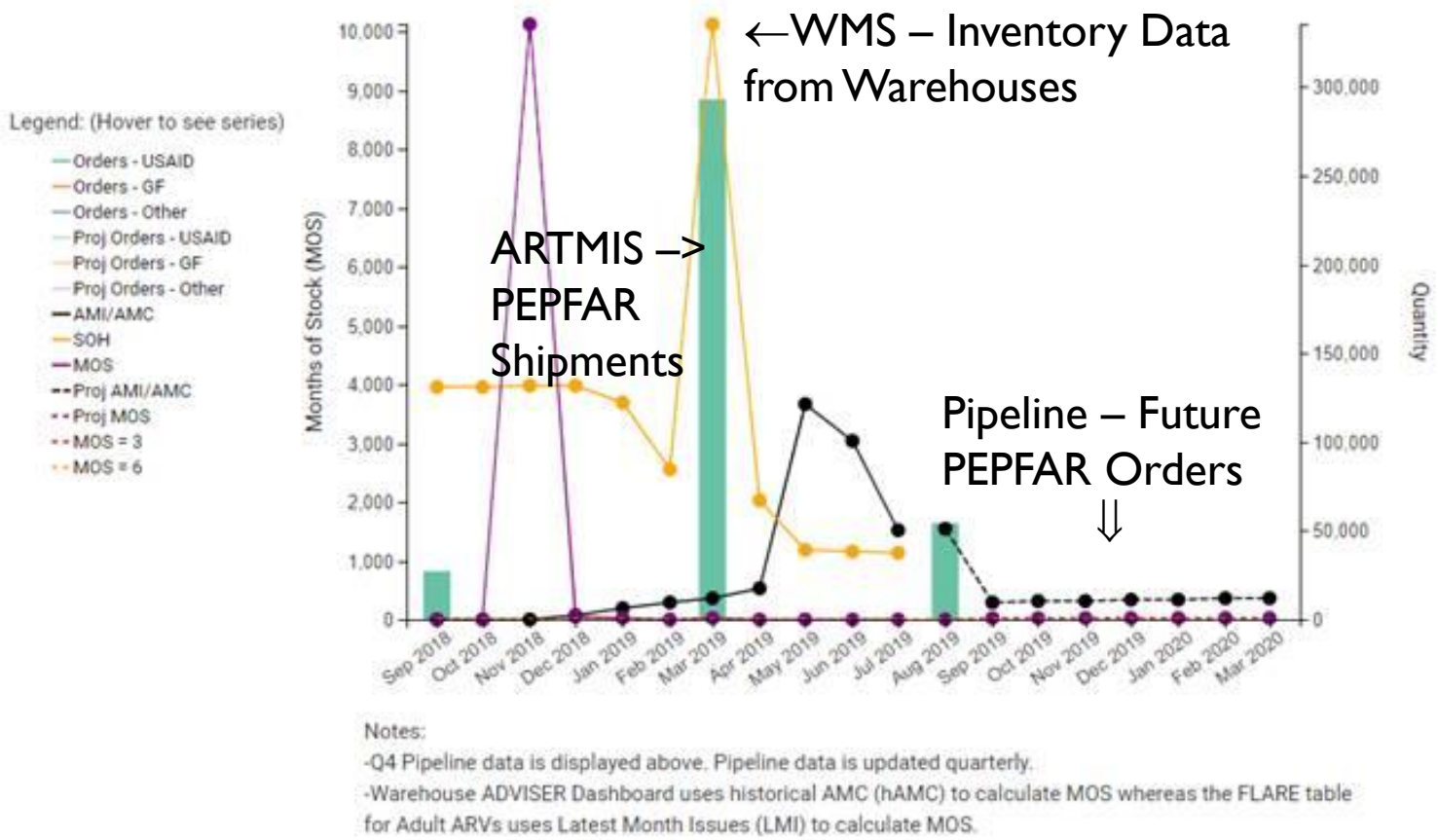
Global View


Warehouse ADVISER - Global
BDI BWA CIV CMR DRC ETH GHA HTI LSO MOZ NAM NGA RWA SWZ UG1 UG2 UG3 VNM ZMB ZWE
3TC 10 MG/ML SOLN NO SYR 240 ML
3TC 10 MG/ML SOLN W/ SYR 240 ML
3TC 150 MG 60 TABS
3TC/AZT 150/300 MG 60 TABS
3TC/AZT 30/60 MG 60 TABS
18.3 Rwanda
8.0 Botswana
1.4 Haiti
3.8 Botswana
49.5 Cote d'Ivoire
21.0 Haiti
0.0 Namibia
19.8 Vietnam
5.1 Zambia
21.7 Burundi
2.9 Botswana
3.5 Cote d'Ivoire
9.1 Cameroon
2.3 DRC
5.1 Ghana
54.8 Haiti
3.5 Lesotho
9.9 Mozambique
4.2 Namibia
11.7 Nigeria
6.7 Rwanda
0.4 eSwatini
3.4 Uganda-JMS
9.3 Uganda-MAUL
0.1 Uganda-NMS
2.9 Vietnam
26.7 Zambia
9.0 Zimbabwe
6.7 Burundi
0.0 Cameroon
17.9 Lesotho
20.4 Rwanda
Hover over each box to learn about the reporting country, selected product, inventory date, and Months of Stock (MOS).
Warehouse ADVISER Dashboard uses historical average monthly consumption (hAMC) to calculate MOS, whereas the FLARE table for Adult ARVs uses Latest Month Issues (LMI) to calculate MOS.
Click on box to Drill down to Country View for the selected product.
Abbreviations: UG1 = Uganda-JMS, UG2 = Uganda-MAUL, UG3 = Uganda-NMS
Legend:
Unknown (AMI=0 & SOH>0)
Stockout (AMI>=0 & SOH=0)
Near Stockout (<3 MOS)
Adequate (3 - 6 MOS)
Overstock (>6 MOS)

Country View

Please select a country, product category, and product from the drop-down menus

Haiti | Select Product Category | Dolutegravir/Lamivudine/Tenofovir DF 50/300/300 mg Tablet, 30 Tabs

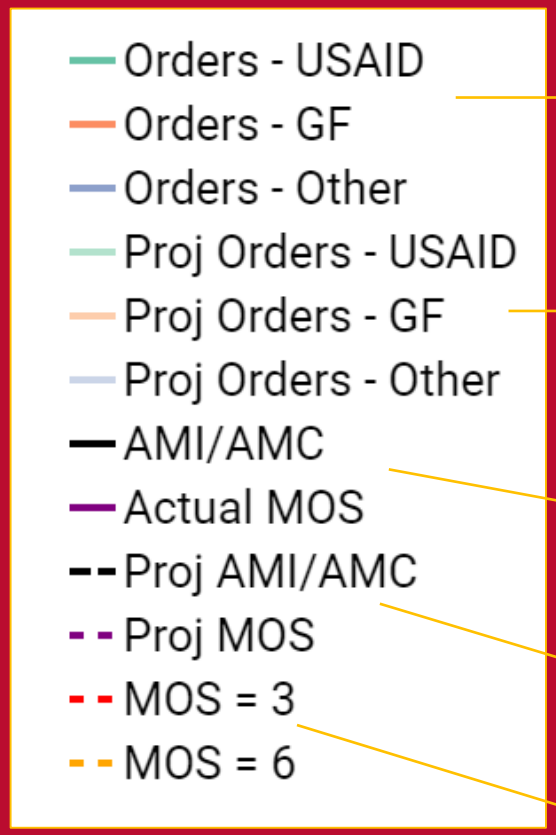


Notes:
-Q4 Pipeline data is displayed above. Pipeline data is updated quarterly.
-Warehouse ADVISER Dashboard uses historical AMC (hAMC) to calculate MOS whereas the FLARE table for Adult ARVs uses Latest Month Issues (LMI) to calculate MOS.

Country Context

Date	Note	Status
Jul 2019	GHSC-PSM shipment (Qty 54,000) was delivered on 8/5/2019 and is not included in SOH. However, we are still understocked as we go on supplying many sites with 7 MOS to enable them to comply with the Multi Month Dispensing policy. Dispensation is increasing to 6 MOS and some sites are even supplying up to 12 MOS to the stable patients. GHSC-PSM shipments (Qty 42,048 and 57,360; 90 Tabs) are expected in October 2019 and January 2020. Orders are also being placed for 180 tabs.	Newly Introduced
Jun 2019	GHSC-PSM shipment (Qty 54,000) is scheduled for August 2019. GHSC-PSM shipment (Qty 42,048) is planned for December 2019. At the end of May, sites had 8.8 MOS. The central level understock is due to the MMD boost strategy and large site level distributions. The next shipments are planend for delivery prior to the next quarterly distribution. This will be the last shipment in FY19 and FY20 as the consumption of 30	Newly Introduced

Warehouse ADVISER: What You Will See



Delivered USAID orders
Delivered GF orders
Delivered Other donors (i.e. government, other donors)

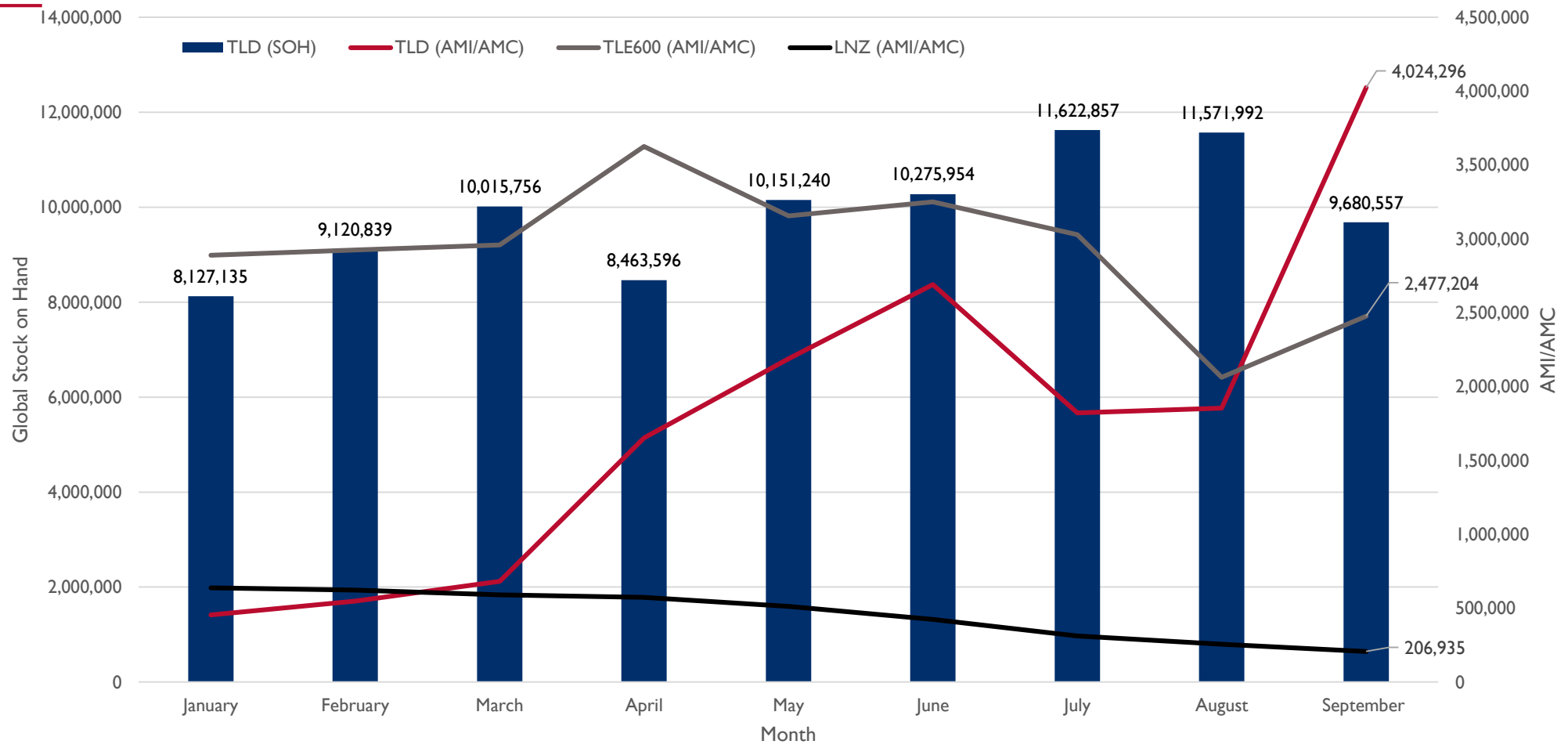
Projected USAID orders (from Q4 Pipeline)
Projected GF orders (from Q4 Pipeline)
Projected Other orders (from Q4 Pipeline)

Average Monthly Issues/Average Monthly Consumption
Actual MOS

Projected AMI/AMC (from Q4 Pipeline)
Projected MOS (from Q4 Pipeline)

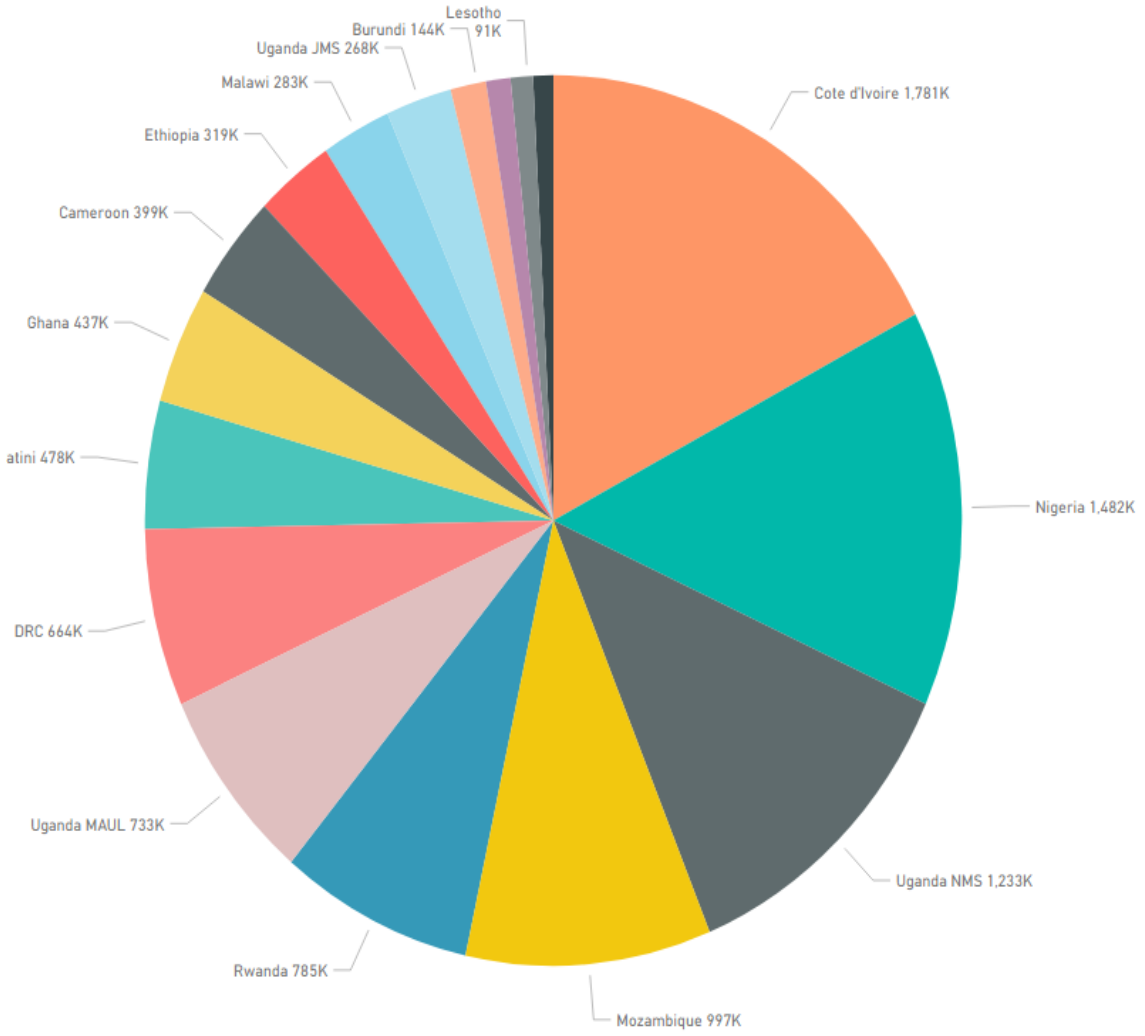
Min/Max for Stock Levels

Global SOH of TLD and AMI/AMC of TLD against Legacy ARVs

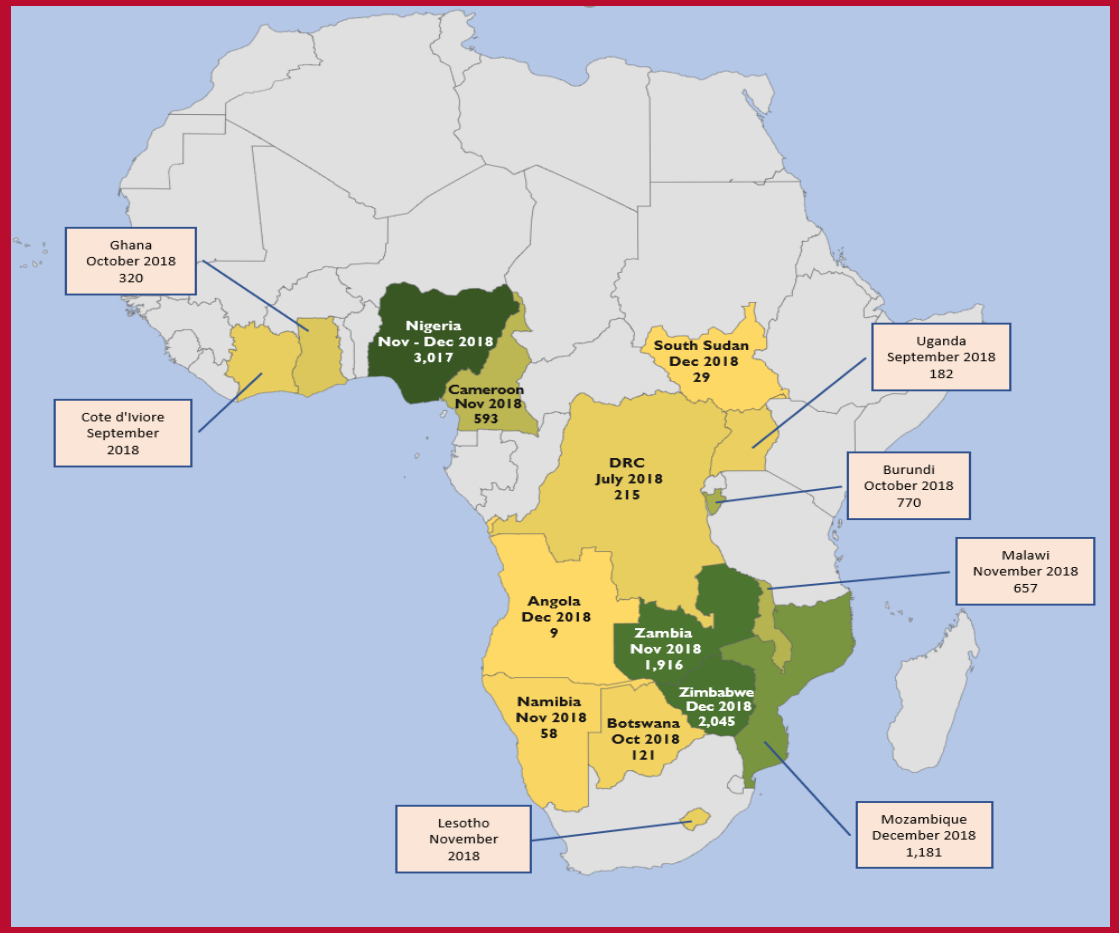


Countries included in this analysis: Botswana, Burundi, Cameroon, Côte d'Ivoire, DRC, Eswatini, Ethiopia, Ghana, Haiti, Lesotho, Mozambique, Namibia, Nigeria, Rwanda, Uganda, Vietnam, Zambia, and Zimbabwe.

TLE 600 SoH Reported as of September 2019 by Country



SC-FACT
Supply Chain – Facility-level AIDS Commodity Tracking



ARVs –
Adult, Pediatric
RTKs
IPT

More than **20 HIV/AIDS Commodities** monitored at **14,000 Service Delivery Points (SDPs)** under **SC-FACT in17** countries since September 2018

SC-FACT Objectives:

DATA REPORTING

To ensure frequent, regular (monthly) availability of facility level stock **data reporting** on monthly basis to USAID to match PEPFAR Quarterly reviews.

- % of countries reporting stock data per plan

To quarterly **reconcile master data** with regard to master facility list and master product list for all reporting countries.

- % of countries with updated master facility and product list

DATA QUALITY

To perform **quality checks** on quarterly basis to validate the stock data.

- % of countries with DQA verified stock data
- % of countries with data irregularities

DATA FOR DECISION MAKING

To **generate excel-based global, country and sub-national dashboards** to promote "data for decision making" at all levels

- % of countries using site-level stock data for commodity security meetings
- % of countries referring/presenting data to develop workplans, TA requests, COP

INFORMATIOM SYSTEMS STRENGTHENING

To **identify gaps/reasons for unavailability of monthly stock data and provide TA/resources** to strengthen/enable site level stock reporting systems

- % of countries enabled using TA/resources

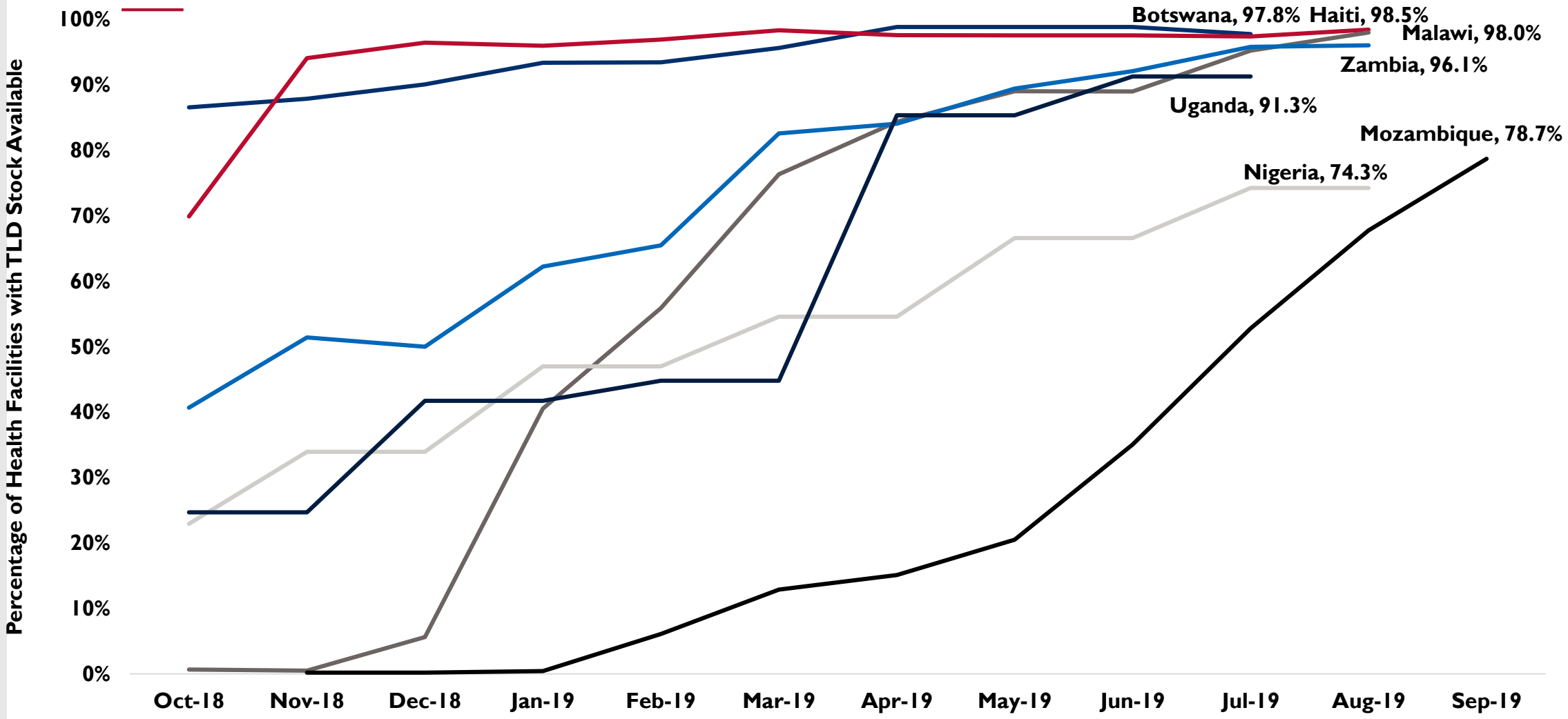
SC-FACT Country Tracker

Country	Status	Data Type	Reporting Frequency	Reporting Lag	Reporting Period	Number of Facilities	Number of Products
Angola	Data Reviewed	1 Excel File	Monthly	One Month	2019-07	9	20
Botswana	Data Reviewed	199 Excel Files	Monthly	One Month	2019-07	136	26
Burundi	Pending Data	---	Monthly		2019-05	---	---
Cameroon	Data Reviewed	1 Excel File	Monthly	One Month	2019-08	620	14
Cote d'Ivoire	Pending Data	---	---	---	---	---	---
DRC	Pending Data	---	---	---	---	---	---
eSwatini	Pending Data	---	---	---	---	---	---
Ethiopia	Pending Data	---	---	---	---	---	---
Ghana	Data Reviewed	---	Monthly	Two Months	2019-06	---	---
Haiti	Data Reviewed	2 Excel Files, 1 PDF	Monthly	One Month	2019-08	257	31
Lesotho	Data Reviewed	1 Excel File	Monthly	One Month	2019-08	210	28
Malawi	Data Reviewed	1 Excel File	Monthly	One Month	2019-08	639	21
Mozambique	Data Reviewed	1 Excel File	Monthly	2-3 weeks	2019-09	1214	26
Namibia	Data Reviewed	57 Excel Files	Monthly	One Month	2019-07	57	29
Nigeria	Data Reviewed	1 Excel File	Once every 2 months	One Month	2019-08	2724	28
Rwanda	Pending Data	---	---	---	---	---	---
South Sudan	Data Reviewed	1 Excel File	Monthly	One Month	---	---	---
Tanzania	Pending Data	---	---	---	---	---	---
Uganda	Data Reviewed	1 Excel File	Once every 2 months	Two Months	2019-07	1644	25
Vietnam	Data Reviewed	2 Excel Files, multiple tabs	Once every 2 months	Two Months	2019-06	---	---
Zambia	Data Reviewed	1 Excel File	Monthly	One Month	2019-07	2132	20
Zimbabwe	Data Reviewed	1 Excel File	Quarterly	One Month	2019-09	1748	26

* Currently not processing

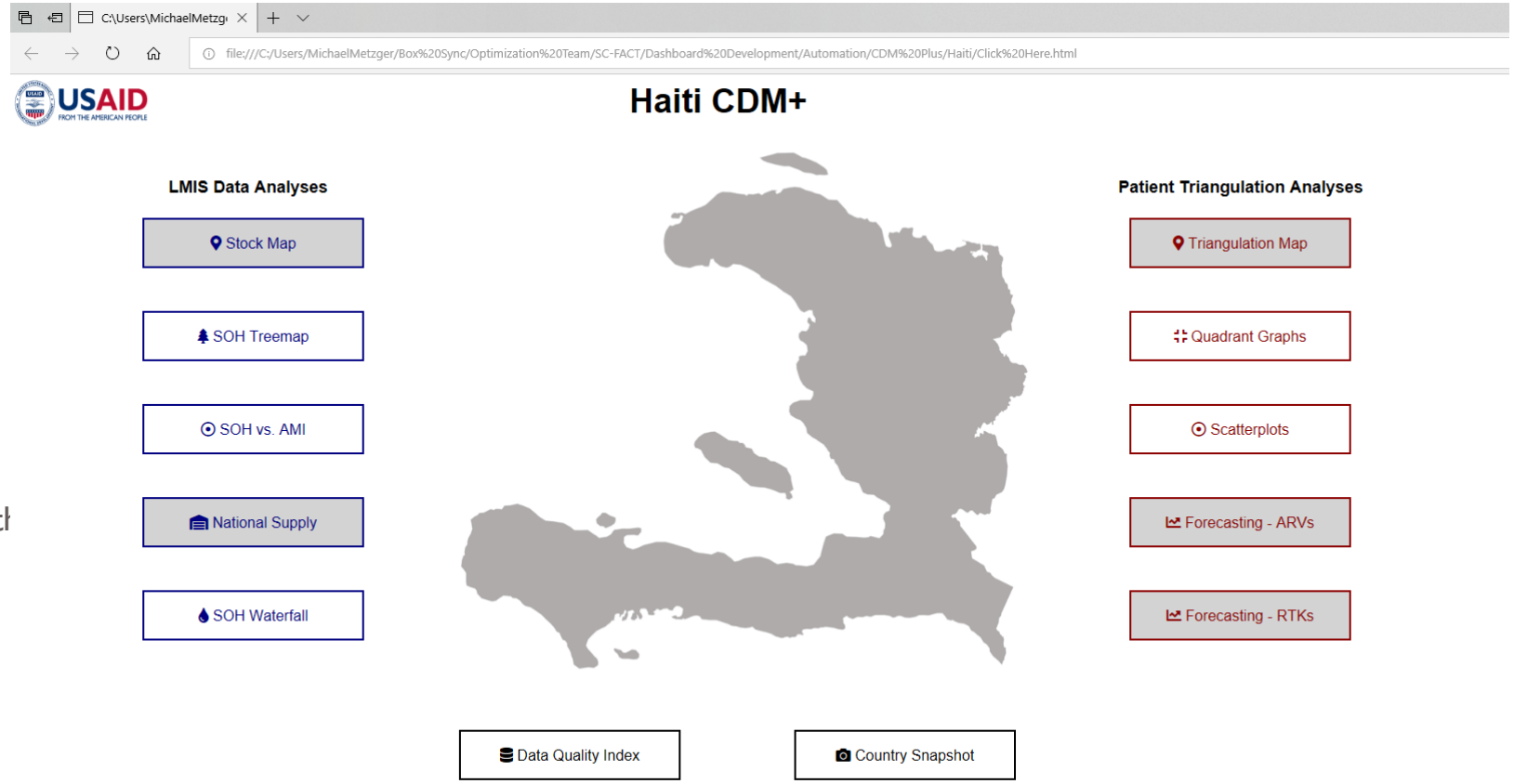
** Aggregated Data

Percentage of Sites Reporting TLD Stocks Availability



Country Diagnostics & Mitigation (CDM) Tool

- **Developed CDMs for 8 Countries:**
  - Botswana
  - Haiti
  - Lesotho
  - Mozambique
  - Namibia
  - Nigeria
  - Zimbabwe
  - Zambia
- **Conducting Workshop:**
  - Enable PMUs and Field Offices to better use th



Data Triangulation

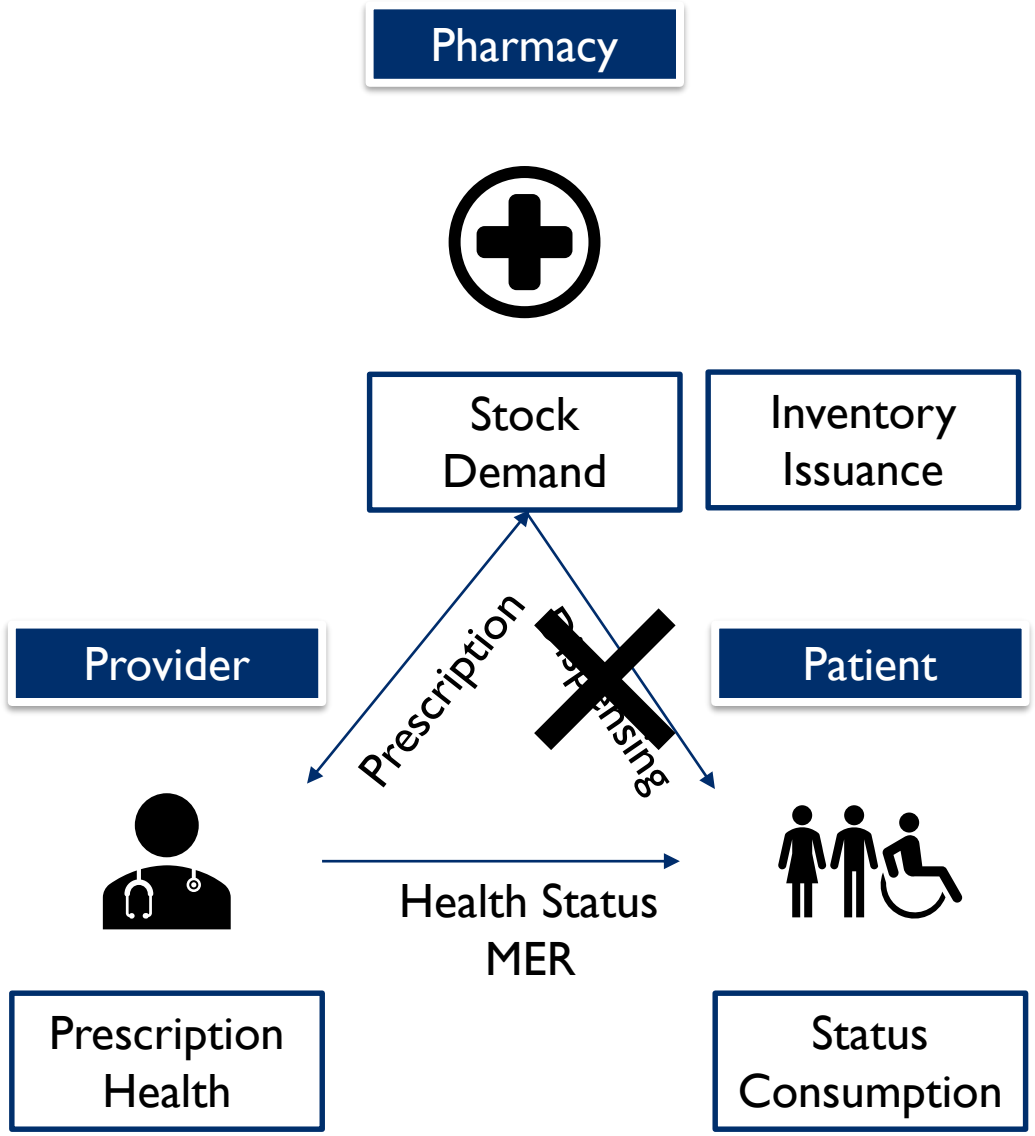
Ideal

- Dispensing data
- Drug regimen
- Prescription pattern
- MMD scaleup
- PrEP
- Testing

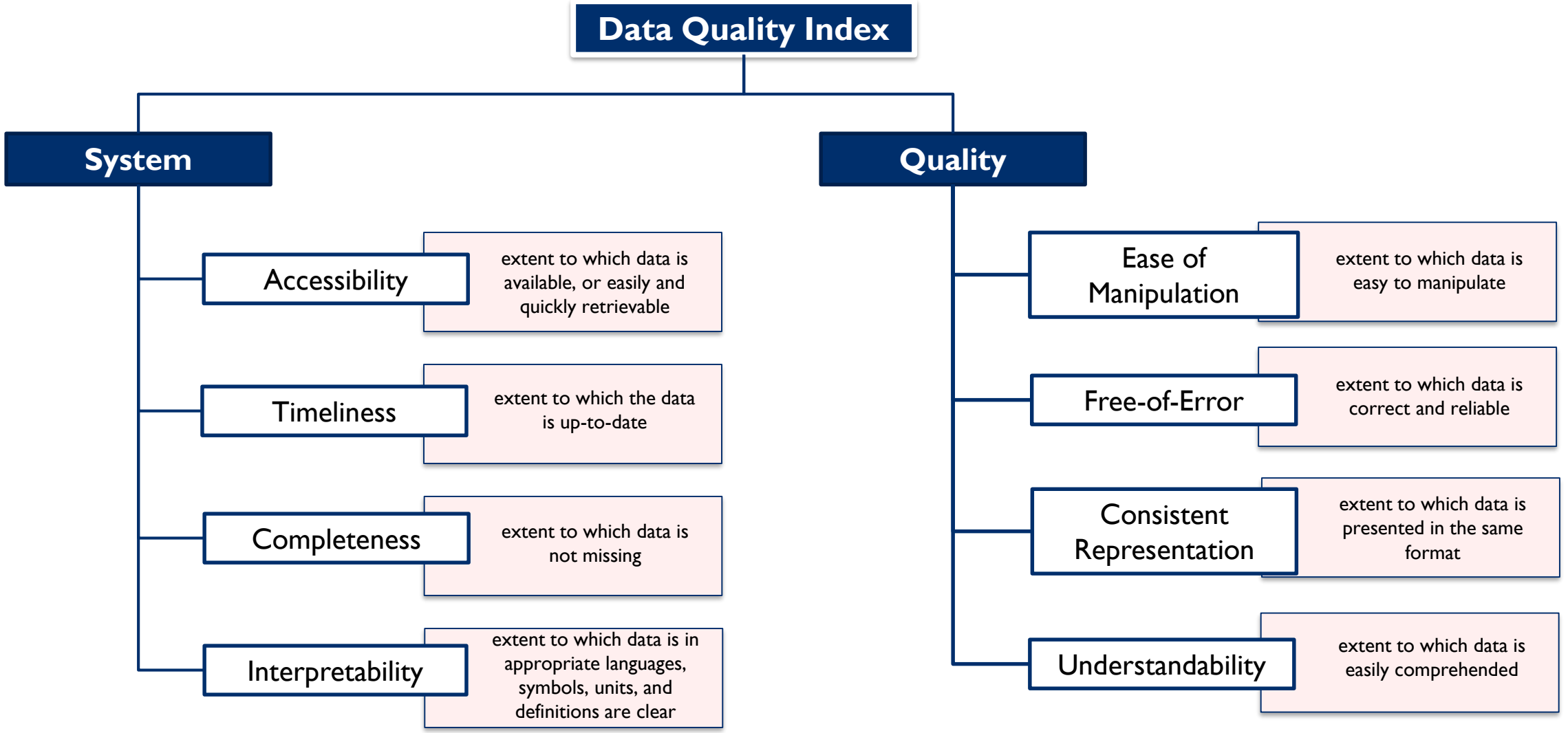
Vs

Reality

- **Issuance with no drug dispensing**



Data Quality Index



Draft Ranking of Tier 1, Tier 2 Countries (weighted scores)

	Zimbabwe	Namibia	Rwanda	Cote d'Ivoire	Lesotho	Haiti	Angola	Mozambique	Nigeria	Zambia
Accessibility	0	10	5	0	10	5	10	10	10	10
Completeness	9.1	3.64	3.64	9.1	7.28	10.92	10.92	9.1	14.56	14.56
Consistent Representation	3.33	0	3.33	0	0	0	3.33	0	3.33	0
Ease of Manipulation	0	3.33	9.99	16.65	0	19.98	13.32	13.32	19.98	16.65
Free-of-Error	0	0	0	0	0	0	0	0	0	0
Interpretability	7.5	5	5	0	10	0	0	5	10	10
Timeliness	0	10	10	10	10	10	10	10	0	5
Understandability	0	5	5	5	5	5	5	5	5	5
Scale	Acceptable	Acceptable	Acceptable	Good	Good	Good	Good	Good	Good	Very Good
Total Weighted Score	34.94	48.79	49.22	51.86	53.10	60.11	61.46	64.32	69.83	75.76

Limitations

- GHSC-PSM in each PEPFAR Country is not the same – **only five countries with LMD**
- Twelve GHSC-PSM FOs budgets have gone down which may affect 'below HQ presence' in countries – such as Botswana
- To be successful, GHSC-PSM link to PEPFAR clinical IPs and HQ clinical teams is critical
- Supply Chain data quality – Relies on clinical IP's inputs,
- PEPFAR funded MER doesn't have unique ID

PharmAssist

Providing Global Support for the PEPFAR Community

Dear PEPFAR Community,

In the wake of the 10th IAS Conference in Mexico City, the USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project's HIV/AIDS team is pleased to introduce *PharmAssist*, a new bimonthly digest to provide timely HIV/AIDS supply chain updates to our global PEPFAR community.

Dear PEPFAR Community,

As we embark on PEPFAR Country Operational Plan-2019 (COP19), the USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project is pleased to announce the second issue of ***PharmAssist***. By sharing health supply chain data at the global level, and by building capacity for local data collection and use, together we can ensure progress toward a patient-centric supply chain to achieve PEPFAR's epidemic control goals. With updates provided here, we hope to support your alignment with


THANKFUL