**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.

<table>
<thead>
<tr>
<th>TIME</th>
<th>TOPIC</th>
<th>SPEAKERS</th>
<th>SLIDE LOCATION</th>
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</thead>
<tbody>
<tr>
<td>Sunday, November 24 (Day 0)</td>
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<tr>
<td>13:00 to 17:00</td>
<td>One on One Sessions</td>
<td></td>
<td>SECOND FLOOR BREAKOUT ROOMS</td>
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<tr>
<td>Coffee from 15:30 to 16:00</td>
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<td>SECOND FLOOR FOYER</td>
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<tr>
<td>Monday, November 25 (Day 1): Forward Demand and Regulatory Matters</td>
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<tr>
<td>Breakfast and Registration from 7:30 to 8:30</td>
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<td>EAST ROOM</td>
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<tr>
<td>Morning Plenary from 8:30 to 13:00</td>
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</tbody>
</table>
| 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, Tson Tsegaye  
                        |                                                 | Republic of South Africa, Khadija Jamaloodien | SLIDE #8  
                        |                                                 | SLIDE #22  
<pre><code>                    |                                                 | SLIDE #36 |
</code></pre>
<table>
<thead>
<tr>
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<th>SPEAKERS</th>
<th>SLIDE LOCATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 to 10:30</td>
<td>Individual Highlights for Each Procurement Channel</td>
<td>UNDP, Zafar Yuldashev, Global Fund, Uranchimeg Badarch, GHSC-PSM, Alan Pringle</td>
<td>SLIDE #53, #66, #82</td>
</tr>
<tr>
<td></td>
<td>Coffee from 10:30 to 11:00</td>
<td></td>
<td>STATE FOYER</td>
</tr>
<tr>
<td>11:00 to 11:30</td>
<td>Five Year WHO-AMDS Forecast</td>
<td>Boniface Nguimfack, WHO, Dr. Adebiiyi Adesina, Avenir Health</td>
<td>SLIDE #92</td>
</tr>
<tr>
<td>11:30 to 13:00</td>
<td>FDA Presentations</td>
<td>Dr. Harinder Chahal, USFDA, Dr. George Lunn, USFDA, Dr. Peter Capella, USFDA, Dr. Sarita Boyd, USFDA, Dr. David Araojo, USFDA, William Lewallen, USFDA</td>
<td>SLIDE #113, #125, #147</td>
</tr>
<tr>
<td>Lunch from 13:00</td>
<td>Coffee from 15:30 to 16:00</td>
<td></td>
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<tr>
<td>14:00 to 18:00</td>
<td>One on One Sessions: The Global Fund, Republic of South Africa, USAID, GHSC-PSM, KEMSA, Ethiopia, PFSA, UNDP, PAHO</td>
<td>SECOND FLOOR BREAKOUT ROOMS</td>
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<tr>
<td>Coffee from 15:30</td>
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<td>SECOND FLOOR FOYER</td>
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<tr>
<td>Tuesday, November 26 (Day 2) - Quality Assurance and Product Optimization</td>
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<tr>
<td>Breakfast from 8:00 to 9:00</td>
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<td></td>
<td>EAST ROOM</td>
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<tr>
<td>Morning Plenary from 9:00 to 12:00</td>
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<tr>
<td>9:00 to 9:30</td>
<td>Quality Assurance: Expectations and Analyses</td>
<td>Dr. Christine Malati, USAID (PEPFAR), Dr. Aida Cancel, GHSC-QA, Hien Dinh, GHSC-QA, Martin Auton, Global Fund</td>
<td>SLIDE #154, #165</td>
</tr>
<tr>
<td>9:30 to 10:00</td>
<td>Updates on Medicines 4 All</td>
<td>Dr. Eugene Choi, Virginia Commonwealth University</td>
<td>SLIDE #166</td>
</tr>
<tr>
<td>Coffee from 10:00</td>
<td></td>
<td></td>
<td>STATE FOYER</td>
</tr>
<tr>
<td>10:30 to 12:00</td>
<td>Future Guidelines and Treatment Optimisation</td>
<td>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)</td>
<td>SLIDE #195, #238, #261</td>
</tr>
<tr>
<td>TIME</td>
<td>TOPIC</td>
<td>SPEAKERS</td>
<td>SLIDE LOCATION</td>
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</tr>
<tr>
<td>Lunch from 12:00 to 13:00</td>
<td></td>
<td>Wesley Kreft, ARV Procurement Working Group</td>
<td>SLIDE #279</td>
</tr>
<tr>
<td>13:00 to 18:00</td>
<td>One on One Sessions: The Global Fund, Republic of South Africa, USAID, GHSC-PSM, KEMSA, Ethiopia PFSA, UNDP, PAHO</td>
<td></td>
<td>SECOND FLOOR BREAKOUT ROOMS</td>
</tr>
<tr>
<td>Coffee from 15:30 to 16:00</td>
<td></td>
<td></td>
<td>SECOND FLOOR FOYER</td>
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<tr>
<td>Wednesday, November 27 (Day 3) – Supply Chain Optimisation</td>
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<tr>
<td>Breakfast from 8:00 to 9:00</td>
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<td></td>
<td>EAST ROOM</td>
</tr>
<tr>
<td>9:00 to 10:00</td>
<td>Grand Ballroom available for use for side meetings.</td>
<td></td>
<td>GRAND BALLROOM</td>
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<tr>
<td>Coffee from 10:00 to 10:15</td>
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<td>STATE FOYER</td>
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<tr>
<td>Morning Plenary 10:15 to 12:30</td>
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<tr>
<td>10:15 to 10:45</td>
<td>18 Month Consolidated Forecast</td>
<td>Chirag Rajpuria, The Global Fund</td>
<td>SLIDE #288</td>
</tr>
<tr>
<td>10:45 to 12:15</td>
<td>Supply Chain Optimisation and Country Uptake</td>
<td>Dr. Messai Belayneh, USAID (PEPFAR) Dr. Christine Malati, USAID (PEPFAR) Khadija Jamaloodien, Republic of South Africa Charles Lwanga, USAID</td>
<td>Kenya (PEPFAR) Mercy Mpatwa, United Republic of Tanzania Dr. Nagesh Borse, GHSC-PSM</td>
</tr>
<tr>
<td>12:25 to 12:45</td>
<td>Closing Remarks</td>
<td>Martin Auton, Global Fund Khadija Jamaloodien, Republic of South Africa Dr. William Paul, US Department of State (PEPFAR)</td>
<td>GRAND BALLROOM</td>
</tr>
<tr>
<td>Lunch from 12:45 to 14:00</td>
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<td>EAST ROOM</td>
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<tr>
<td>14:00 to 17:00</td>
<td>One on One Sessions: The Global Fund, Republic of South Africa, USAID, GHSC-PSM, KEMSA, Ethiopia PFSA, UNDP, PAHO</td>
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<td>SECOND FLOOR FOYER</td>
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ARV Buyer Seller Coordinated Demand Visibility Update

November 2019
Washington, DC
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

<table>
<thead>
<tr>
<th>ARV Transitions are Occurring at a Rapid Rate</th>
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<tbody>
<tr>
<td>- 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</td>
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<tr>
<td>- This has led to shorter production life cycles for ARVs, down to 3 years and less in some cases.</td>
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<table>
<thead>
<tr>
<th>Accuracy and Demand Visibility</th>
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<tbody>
<tr>
<td>- Agreement to share more analysis on forecast accuracy</td>
</tr>
<tr>
<td>- Looking to share more firm demand for new ARVs that are required for optimization efforts</td>
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<tr>
<td>- Interest in sharing more data to show the decrease or “phase-out” of legacy ARVs that are being replaced</td>
</tr>
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<table>
<thead>
<tr>
<th>Interest in Ensuring Decreasing Shelf-Life Requirements for Importation</th>
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<tbody>
<tr>
<td>- Participants agreed that efforts are needed to reduce shelf-life requirements for the importation of ARVs</td>
</tr>
<tr>
<td>- This will increase supply chain efficiency and flexibility; and regularity of deliveries</td>
</tr>
<tr>
<td>- 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</td>
</tr>
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</table>
ARVs Large Buyers/Sellers Forum

Kenya Presentation

By Douglas Onyancha
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

**Kenya HIV Estimates, 2018**

- **HIV Prevalence** = 4.9%
  - Female = 6.2%
  - Male = 3.5%
- **PLHIV (all ages)** = 1.5M
- **Adolescents and Young People**
  - Adolescents 10-19 years
    - All ages = 52,800
    - PLHIV = 105,200
    - New infections = 8,200
  - Young Adults 15-24 years
    - PLHIV = 184,700
    - New infections = 17,700
- **Number of new HIV Infections in 2017**
  - Adults (15+) = 44,800
  - Children (0-14) = 8,000

New estimates expected before end of year after release of KENPHIA Results
Patient Scale up

Patient numbers


980,000  990,000  1,000,000  1,010,000  1,020,000  1,030,000  1,040,000  1,050,000  1,060,000  1,070,000  1,080,000

1,008,777  1,016,561  1,027,134  1,039,404  1,039,405  1,054,711  1,052,128  1,065,805

www.kems.co.ke
Email: info@kems.co.ke, sales@kems.co.ke  kemskenya  @Kems_Kenya
Trends: National ART Regimens

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

Key 1st Line Regimens
- TDF-based regimens, 931,520, 97%
- AZT-based regimens, 16,960, 2%
- ABC Based regimens, 6,294, 1%
- Other 1st Line, 5,103, 0%

Key 2nd Line Regimens
- TDF-based regimens, 47,404, 51%
- AZT-based regimens, 38,542, 42%
- Other 2nd Line, 6,078, 7%

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

<table>
<thead>
<tr>
<th>Age/Weight</th>
<th>Preferred Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth – 4 weeks</td>
<td>AZT + 3TC + RAL1</td>
</tr>
<tr>
<td>&lt; 20 kg (above 4 weeks old)</td>
<td>ABC² + 3TC + LPV/r</td>
</tr>
<tr>
<td>20 kg – 35 kg</td>
<td>ABC² + 3TC + DTG</td>
</tr>
<tr>
<td>&gt; 35 kg</td>
<td>TDF² + 3TC + DTG</td>
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Procurement

Procurement process is dependent on the 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

<table>
<thead>
<tr>
<th>FY</th>
<th>16/17</th>
<th>17/18</th>
<th>18/19</th>
<th>19/20</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOK-Counterpart Funding</td>
<td>$8,536,000</td>
<td>$7,024,082</td>
<td>6,225,000</td>
<td>$9,986,600.</td>
</tr>
<tr>
<td>Global Fund</td>
<td>$62,561,128</td>
<td>$55,423,864</td>
<td>$17,759,635</td>
<td>$59,933,828</td>
</tr>
<tr>
<td>PEPFAR</td>
<td>$92,000,000</td>
<td>$78,301,486</td>
<td>63,798,699</td>
<td>$44,542,916</td>
</tr>
</tbody>
</table>
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)
Your Partner in HealthCare

Thank You

www.kemsa.co.ke

Email: info@kemsa.co.ke, sales@kemsa.co.ke
Ethiopia’s update on HIV program and procurement

Washington DC

The Mayflower Hotel
November 24-27, 2019
• 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

• Ethiopia is a Federal State having nine regional states and two City Administrations

• In 2017, total projected population: 94,351,001 (CSA 2017)
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.

ARV Budget July 2016 to June 2021

- July 2016 to June 2017: 62,359,840.47
- July 2017 to June 2018: 53,942,191
- July 2018 to June 2019: 48,126,389
- July 2019 to June 2020: 53,060,495
- July 2020 to June 2021: 52,180,491
Current ARVs Procurement for 2019/20

- GF PPM: $1,133,866.54
- EPSA SPOT TENDERING: $18,863,979.52
- EPSA LTA: $33,159,947.01
Procurement Expenditure 2019/20

ABC/3TC - 120mg/60mg Tab
ABC 300mg
ATV/r
DRV-150mg Tab
DRV-600mg Tab
DRV-75mg Tab
DTG
TLD of 30
TLD of 90
3TC
LPV/r 40mg/10mg
LPV/r 100mg/25mg
LPV/r 200mg/50mg
RAL-100mg Tab
RTV-100mg Tab
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

### Performance evaluation scoring
- **Excellent performance** - 90-100%
- **Very good performance** - 80-89%
- **Good performance** - 70-79%
- **Fair performance** - 60-69%
- **Poor performance** <60%

<table>
<thead>
<tr>
<th>Scoring element</th>
<th>Weight</th>
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<tbody>
<tr>
<td>Supplier lead time</td>
<td>50%</td>
</tr>
<tr>
<td>Line fill rate</td>
<td>30%</td>
</tr>
<tr>
<td>Responsiveness</td>
<td>20%</td>
</tr>
</tbody>
</table>
# Line fill rate evaluation

<table>
<thead>
<tr>
<th>No.</th>
<th>Item Description</th>
<th>Quantity</th>
<th>Received QTY</th>
<th>Line Fill Rate%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ABC+3TC-120mg+60mg-Tablet</td>
<td>87.646</td>
<td>87.646</td>
<td>100.0%</td>
</tr>
<tr>
<td>2</td>
<td>ATV/r-300mg+100mg-Tablet</td>
<td>284.901</td>
<td>284.901</td>
<td>100.0%</td>
</tr>
<tr>
<td>3</td>
<td>DRV-600mg-Tablet</td>
<td>6.194</td>
<td>6.194</td>
<td>100.0%</td>
</tr>
<tr>
<td>4</td>
<td>DTG-50mg-Tablet</td>
<td>208.062</td>
<td>208.062</td>
<td>100.0%</td>
</tr>
<tr>
<td>5</td>
<td>EFV-200mg-Tablet</td>
<td>19.852</td>
<td>19.852</td>
<td>100.0%</td>
</tr>
<tr>
<td>6</td>
<td>EFV-50mg-Tablet</td>
<td>29.436</td>
<td>29.436</td>
<td>100.0%</td>
</tr>
<tr>
<td>7</td>
<td>TLD</td>
<td>2,200.091</td>
<td>2,200.011</td>
<td>100.0%</td>
</tr>
<tr>
<td>8</td>
<td>TDF+3TC-300mg+300mg-Tablet</td>
<td>309.575</td>
<td>309.575</td>
<td>100.0%</td>
</tr>
<tr>
<td>9</td>
<td>AZT+3TC-150mg+300mg-Tablet</td>
<td>167.957</td>
<td>101.220</td>
<td>60.3%</td>
</tr>
<tr>
<td>10</td>
<td>AZT+3TC-30mg+60mg-Tablet</td>
<td>16.693</td>
<td>16.693</td>
<td>100.0%</td>
</tr>
<tr>
<td>11</td>
<td>3TC-150mg-Tablet</td>
<td>18.778</td>
<td>18.778</td>
<td>100.0%</td>
</tr>
<tr>
<td>12</td>
<td>LPV/r-200mg+50mg-Tablet</td>
<td>33.213</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>13</td>
<td>LPV/r-100mg+25mg-Tablet</td>
<td>90.078</td>
<td>9.078</td>
<td>100.0%</td>
</tr>
<tr>
<td>14</td>
<td>NVP-10mg/ml-suspension</td>
<td>13.662</td>
<td>13.662</td>
<td>100.3%</td>
</tr>
<tr>
<td>15</td>
<td>RTV-25mg-Tablet</td>
<td>58.17</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>16</td>
<td>RTV-100mg-Tablet</td>
<td>61.94</td>
<td>6.194</td>
<td>100.0%</td>
</tr>
<tr>
<td>17</td>
<td>AZT-10mg/ml-solution</td>
<td>92.250</td>
<td>92.250</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

**Average line fill rate**: 85.9%
## Lead time evaluation

<table>
<thead>
<tr>
<th>PD</th>
<th>Item Description</th>
<th>Quantity</th>
<th>L/C/CAO Opening date</th>
<th>Shipped Quantity</th>
<th>Date of shipment</th>
<th>Lead time (Days)</th>
<th>Average Lead time (Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>ATV/r-300mg+100mg-Tablet</td>
<td>113,960</td>
<td>19-Feb-19</td>
<td>113,960</td>
<td>30-Mar-19</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>b</td>
<td>3TC-150mg-Tablet</td>
<td>18,778</td>
<td>30-Jan-19</td>
<td>8,771</td>
<td>15-Feb-19</td>
<td>54</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td>AZT+3TC-30mg+60mg-Tablet</td>
<td>16,693</td>
<td></td>
<td>10,007</td>
<td>25-Mar-19</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AZT+3TC-150mg+300mg-Tablet</td>
<td>100,774</td>
<td></td>
<td>14,620</td>
<td>15-Feb-19</td>
<td>16</td>
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<tr>
<td></td>
<td>EFV-200mg-Tablet</td>
<td>19,852</td>
<td>31-Jan-19</td>
<td>19,852</td>
<td>5-Apr-19</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EFV-50mg-Tablet</td>
<td>29,436</td>
<td></td>
<td>7,500</td>
<td>5-Feb-19</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF+3TC-300mg+300mg-Tablet</td>
<td>123,830</td>
<td>22-May-19</td>
<td>123,830</td>
<td>18-Jul-19</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AZT+3TC-150mg+300mg-Tablet</td>
<td>41,989</td>
<td></td>
<td>41,989</td>
<td>4-Jul-19</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>DRV-600mg-Tablet</td>
<td>6,194</td>
<td>31-Jan-19</td>
<td>2,050</td>
<td>25-Mar-19</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DTG-50mg-Tablet</td>
<td>22,396</td>
<td></td>
<td>4,144</td>
<td>22-May-19</td>
<td>111</td>
<td></td>
</tr>
<tr>
<td>e</td>
<td>DTG-50mg-Tablet</td>
<td>185,666</td>
<td>23-May-19</td>
<td>22,396</td>
<td>4-Jun-19</td>
<td>124</td>
<td></td>
</tr>
<tr>
<td>f</td>
<td>TLD</td>
<td>20,055</td>
<td>31-Jan-19</td>
<td>20,055</td>
<td>26-May-19</td>
<td>85</td>
<td></td>
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<tr>
<td>g</td>
<td>LPV/r-200mg+50mg-Tablet</td>
<td>33,213</td>
<td></td>
<td>34,310</td>
<td>18-Jul-19</td>
<td>56</td>
<td></td>
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<tr>
<td>h</td>
<td>TLD</td>
<td>1,300,000</td>
<td>30-Jan-19</td>
<td>769,950</td>
<td>18-Mar-19</td>
<td>47</td>
<td>85</td>
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<tr>
<td>PO</td>
<td>Item Description</td>
<td>Quantity</td>
<td>L/C/CAD Opening date</td>
<td>Shipped Quantity</td>
<td>Date of shipment</td>
<td>Lead time (Days)</td>
<td>Average Lead time (Days)</td>
</tr>
<tr>
<td>----</td>
<td>----------------------------------</td>
<td>----------</td>
<td>----------------------</td>
<td>------------------</td>
<td>-----------------</td>
<td>------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>i</td>
<td>ATV/r-300mg+100mg-Tablet</td>
<td>79,458</td>
<td>25-Jan-19</td>
<td>79,458</td>
<td>2-Feb-19</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>i</td>
<td>abacavir-300mg- tablet</td>
<td>52,370</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i</td>
<td>ATV/r-300mg+100mg-Tablet</td>
<td>91,483</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>j</td>
<td>TLD</td>
<td>880,036</td>
<td>22-May-19</td>
<td>210,392</td>
<td>11-Aug-19</td>
<td>81</td>
<td>49.5</td>
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<tr>
<td></td>
<td>TDF+3TC-300mg+300mg-Tablet</td>
<td>185,745</td>
<td></td>
<td>185,745</td>
<td>14-Jun-19</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AZT+3TC-150mg+300mg-Tablet</td>
<td>25,194</td>
<td></td>
<td>25,194</td>
<td>29-Jun-19</td>
<td>38</td>
<td></td>
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<tr>
<td></td>
<td>LPV/r-100mg+25mg-Tablet</td>
<td>9078</td>
<td></td>
<td>9,078</td>
<td>7-Aug-19</td>
<td>77</td>
<td></td>
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<tr>
<td>k</td>
<td>ABC+3TC-120mg+60mg-Tablet</td>
<td>35,276</td>
<td>30-Jan-19</td>
<td>35,276</td>
<td>6/29/2019</td>
<td>150</td>
<td>160</td>
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<tr>
<td></td>
<td>NVP-10mg/ml-suspension</td>
<td>13,622</td>
<td></td>
<td>13,662</td>
<td>6/29/2019</td>
<td>150</td>
<td></td>
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<tr>
<td></td>
<td>RIV-25mg-Tablet</td>
<td>5,817</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>l</td>
<td>AZT-10mg/ml-solution</td>
<td>50,000</td>
<td>25-Mar-19</td>
<td>50,000</td>
<td>30-Mar-19</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>m</td>
<td>AZT-10mg/ml-solution</td>
<td>42,250</td>
<td>4-Jul-19</td>
<td>42,250</td>
<td>11-Sep-19</td>
<td>69</td>
<td>67.5</td>
</tr>
<tr>
<td>n</td>
<td>RIV-100mg-Tablet</td>
<td>6194</td>
<td>30-Mar-19</td>
<td>6,194</td>
<td>7-Jun-19</td>
<td>69</td>
<td>69</td>
</tr>
</tbody>
</table>

**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!!!
Ms Khadija Jamaloodien
Affordable Medicines Directorate

Republic of South Africa

ARV Large Buyer Seller Summit
November 2019
Day 1
Contents

1. HIV & AIDS in South Africa
2. Approach to procurement
3. Forecasted patients on ART
4. TLD transition
HIV & AIDS in South Africa

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

**Department of Health has set aggressive growth targets for this year**

**Source**
- Thembisa 4.2 model
- 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

1. HIV & AIDS in South Africa

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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

1. HIV & AIDS in South Africa
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3. Forecasted patients on ART
4. TLD transition
Adults on 1st line ART

Source: Team analysis; TEE/TLD profile based on input from provinces together with modelling of qualifying patients
## Regimen split: 2nd line adults

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

Source: Team analysis; based on latest ARV guidelines (awaiting sign-off)
## Regimen split: 1st line children

<table>
<thead>
<tr>
<th></th>
<th>Dec-19</th>
<th>Dec-20</th>
<th>Dec-21</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/3TC+EFV</td>
<td>92,889</td>
<td>17,058</td>
<td>16,563</td>
<td>Expectation that EFV &amp; LPV/r will be replaced by DTG 50</td>
</tr>
<tr>
<td>ABC/3TC+LPV/r</td>
<td>46,621</td>
<td>7,697</td>
<td>6,604</td>
<td></td>
</tr>
<tr>
<td>ABC/3TC+DTG</td>
<td>1,710</td>
<td>129,031</td>
<td>139,691</td>
<td></td>
</tr>
<tr>
<td>AZT/3TC+NVP</td>
<td>6,338</td>
<td>6,371</td>
<td>6,403</td>
<td></td>
</tr>
<tr>
<td>ABC/3TC+ATV/r</td>
<td>3,375</td>
<td>945</td>
<td>1,244</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>150,933</strong></td>
<td><strong>161,102</strong></td>
<td><strong>170,504</strong></td>
<td></td>
</tr>
</tbody>
</table>
1. HIV & AIDS in South Africa
2. Approach to procurement
3. Forecasted patients on ART
4. TLD transition
Status of TLD transition

- 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

Official launch by Minister planned for 27 November 2019
### National demand plan

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

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

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

*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
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
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. Services account for 70% of total UN procurement.

Procurement Trend (Million USD)
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
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 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**
### LIST OF ADULT ARVS (UNDER LTAS)

<table>
<thead>
<tr>
<th>Product</th>
<th>Quantity</th>
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</thead>
<tbody>
<tr>
<td>Abacavir, 300 mg, 60 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Abacavir/Lamivudine, 600mg+300mg, 30 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Atazanavir/Ritonavir, 300mg+100mg, 30 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Darunavir, 400mg, 60 Tab Bottle</td>
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</tr>
<tr>
<td>Darunavir, 600mg, 60 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Efavirenz, 600mg, Blister of 10-30(3+10)</td>
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</tr>
<tr>
<td>Efavirenz, 600mg, 30 Tab Bottle</td>
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<tr>
<td>Efavirenz/Lamivudine/Tenofovir, 600mg+200mg+300mg, 30 Tab Bottle</td>
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</tr>
<tr>
<td>Efavirenz/Lamivudine/Tenofovir, 400mg+300mg+300mg, 30 Tab Bottle</td>
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</tr>
<tr>
<td>Efavirenz/Lamivudine/Tenofovir, 400mg+300mg+300mg, 90 Tab Bottle</td>
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<tr>
<td>Efavirenz/Lamivudine/Tenofovir, 600mg+300mg+300mg, 90 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Emtricitabine/Tenofovir, 200mg+300mg, 30 Tab Bottle</td>
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</tr>
<tr>
<td>Lamivudine/Nevirapine/Zidovudine 150mg+200mg+300mg, 60 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Lamivudine/Tenofovir Disoproxyl 300mg+300mg, 30 Tab Bottle</td>
<td></td>
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<tr>
<td>Lamivudine/Zidovudine 150mg+300mg, 60 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Lopinavir/Ritonavir, 200mg+50mg, 120 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Nevirapine, 200mg, 60 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Ritonavir, 100mg, 30 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Tenofovir disoproxil, 300mg, 30 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Zidovudine, 300mg, 60 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Dolutegravir, 50mg, 30 Tab Bottle</td>
<td></td>
</tr>
<tr>
<td>Dolutegravir/Lamivudine/Tenofovir, 50mg+300mg+300mg, 30 Tab Bottle</td>
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</tr>
<tr>
<td>Dolutegravir/Lamivudine/Tenofovir, 50mg+300mg+300mg, 90 Tab Bottle</td>
<td></td>
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</tbody>
</table>
ARV VOLUMES (ADULT)

ARV procurement 2018

- Efavirenz/Lamivudine/Tenofovir, 400+300+300mg-30 Tab bt
- Dolutegravir/Lamivudine/Tenofovir, 50+300+300-30 Tab bt
- Efavirenz/Lamivudine/Tenofovir, 600+300+300mg-30 Tab bt
- Abacavir/Lamivudine, 600mg+300mg-30 Tab bt
- Lopinavir/Ritonavir, 200mg+50mg
- Atazanavir/Ritonavir, 300mg+100mg-30 Tab bt
- Lamivudine/Nevirapine/Zidovudine, 150+200+300mg-60 Tab bt
- Lamivudine/Zidovudine, 150mg+300mg-60 Tab bt
- Emtricitabine/Tenofovir, 200mg+300mg-30 Tab bt
- Efavirenz/Emtricitabine/Tenofovir, 600mg+200mg+300mg

ARV procurement - 2019

- Dolutegravir/Lamivudine/Tenofovir, 50+300+300mg-30 Tab bt
- Atazanavir/Ritonavir, 300mg+100mg-30 Tab bt
- Efavirenz/Lamivudine/Tenofovir, 600+300+300mg-30 Tab bt
- Lamivudine/Zidovudine, 150mg+300mg-60 Tab bt
- Lopinavir/Ritonavir, 200mg+50mg-30 Tab bt
- Efavirenz/Emtricitabine/Tenofovir, 600+200+300mg-30 Tab bt
- Abacavir/Lamivudine, 600mg+300mg-30 Tab bt
- Lamivudine/Tenofovir Disproxyl, 300mg+300mg-30 Tab bt
- Efavirenz, 600mg-30 Tab bt
- Darunavir, 600mg-60 Tab bt
- Lamivudine/Nevirapine/Zidovudine, 150+200+300mg-60 Tab bt

ARV procurement 2018

$0.00 $40,000,000.00 $80,000,000.00

ARV procurement - 2019

-$ $4,000,000 $8,000,000 $12,000,000 $16,000,000
## PROJECTION FOR NEW LTAS

<table>
<thead>
<tr>
<th>Product description</th>
<th>Strength</th>
<th>Dosage form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>300 mg</td>
<td>Tablet</td>
</tr>
<tr>
<td>Abacavir/Lamivudine</td>
<td>600 mg + 300 mg</td>
<td>Tablet</td>
</tr>
<tr>
<td>Abacavir/Dolutegravir/Lamivudine</td>
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<tr>
<td>Atazanavir/Ritonavir</td>
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<td>Lamivudine/Tenofovir disoproxyl fumarate</td>
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<td>Tablet</td>
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<tr>
<td>Lamivudine/Zidovudine</td>
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<td>Tablet</td>
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<tr>
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<td>Nevirapine</td>
<td>200 mg</td>
<td>Tablet</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>400 mg</td>
<td>Tablet</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>100 mg</td>
<td>Tablet</td>
</tr>
<tr>
<td>Tenofovir disoproxyl fumarate</td>
<td>300 mg</td>
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</tr>
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</table>
NEW PROCESS TO ESTABLISH LTAS
(TENDER WILL BE ANNOUNCED IN DECEMBER)
Results supported by UNDP-managed Global Fund grants since 2003

- 3.1 million lives saved
- 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
- 53 countries
- 1.4 million people receiving HIV treatment
- 47 million people counselled and tested for HIV
THANK YOU!!!

zafar.yuldashev@undp.org

Visit http://open.undp.org
Global Fund update and priorities.  
Antiretroviral Large Buyers and Sellers Forum 2019

24 - 27 NOVEMBER 2019  
WASHINGTON DC
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
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

**Spot tender (before 2014)**
- Price centric focus
- Poor performance were reported and not yet managed

**Performance Based Approach (2015-2017)**
- Annual volume allocation and commitment
- Two types of Long term agreements (LTA) with suppliers
- 6 month demand rolling forecast
- Price roadmap
- Rigorous supplier performance management to inform volume allocation and commitment adjustment

**Value creation through SRM (2018-2019)**
- Focus on the strategic areas of 2nd phase of Market Shaping Strategy implementation
- Enhance supplier performance management matrix to inform sound decision making
- Deploy a set of measures to mitigate supply risks, increase supply visibility and prompt best practices
- Establishing direct suppliers relationships with originators

**Cross-disease strategy (2020-2021)**
- New cross-disease strategy: Not only HIV, at least malaria
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**
- **B** An average **16% price reduction for first-line ARV regimen in 2018-2019**
- **C** Increase in **OTIF (on-time-in-full delivery)** to **90%** in 2018-2019 through PPM
- **D** **More responsive supply**: shorter lead-times, VMI and stock visibility for low volume products and stock-outs
- **E** 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
- **More proactive management of quality** and other risks
  - De-risking API/KSM supply
  - Encouraging participation in WHO collaborative and regional pooled registration initiatives
- **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
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.

**Partnership**

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

**Added value**

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

**Economy of scale**

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

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

Invoices
Deliveries
Orders
Access
Compliance

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

<table>
<thead>
<tr>
<th>OTIF</th>
<th>Manufacturer</th>
<th>90% target</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Responsiveness</th>
<th>Manufacturer</th>
<th>80% target</th>
</tr>
</thead>
</table>
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

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

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
- KSM may have impact on supplier security and cost

Intermediate (INT)
- Registered Intermediate (INT) and APIs in the FPP dossier

Active Pharmaceutical Ingredients (API)
- Name /CAS number
- Supplier information
- 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;
  - Variation approval with regards to new API/INT suppliers or new INTs

Information required
- Name /CAS number
- Supplier information including current registered supplier and suppliers are in the process with indicative approval timeline
- others

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
- Tender outcome informs the initial allocation base
- Supplier allocation base revised based on performance compared to target
- Volume pool created from under performance

### Phase II
Reallocate pooled volume
- Reallocate pool volume through defined mechanism based on over-performance

### Phase III
Implementation risk assessment
- Range of risk factors considered including quality & other implementation constraints (pricing, registration footprint, long lead-times)
- Allocation finalized with risk mitigation plan

### Phase IV
Performance mgmt. & allocation adjustment
- 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.

Sourcing & Management of Health Products

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.

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

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.

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

6,000+ SHIPPING LANES

5 INTERNATIONAL FREIGHT FORWARDERS

300+ SUPPLIERS

1,200 COUNTRY OFFICE STAFF

43 COUNTRIES received technical assistance

17 DELIVERIES* every day

4,000+ ITEMS in the product catalog

$249.7 M PROCURED through local channels

34% LINE ITEMS procured through local channels
Forecasting Increasingly Driven by Data Analytics

- Suppliers – Information shared on a Quarterly Basis
- Forecasting and Supply Planning Team – Quality Check
- Plan Team – Global Aggregation and Order Planning
- Country Based Supply Plans

Data Quality Check
Automation and Feedback

Modeling of Transitions

Scenario Planning
ARV Sourcing Strategies Driven by Product Characteristics

Long Term Agreements (LTA)

- Contracts establish working terms and conditions between the legal entities

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

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

Timing of Sourcing Events

- Multi-Year w Options
  - Quarterly
- Standard Procurements - Allocation
  - Annually

Regular market interaction for TLD and predictable sourcing elsewhere satisfies dynamic product needs.
# Data Driven Proactive Order Management Process

<table>
<thead>
<tr>
<th>Product Group</th>
<th>Sub Category</th>
<th>Country</th>
<th>Product ID</th>
<th>PSM SKU</th>
<th>Product Name</th>
<th>Requested Delivery Date</th>
<th>Target Order Entry Date</th>
<th>Time to Order (Weeks)</th>
<th>Order Type</th>
<th>Max Lead Time (Weeks)</th>
<th>Funds</th>
<th>Quantity</th>
<th>Shipment MOS</th>
<th>UOM StartBalance</th>
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<td>441,894</td>
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</table>
Catalogue Management Driving Optimized Formulary

![Bar chart showing percentage of line items by delivery date and tier]

- Tier 1
- TLD 30
- Tier 2
- TLE
- Not Listed

Delivery Date:
- 2010
- 2011
- 2012
- 2013
- 2014
- 2015
- 2016
- 2017
- 2018
- 2019
- 2020

Percent of Line Items:
- 0%
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%
- 70%
- 80%
- 90%
- 100%
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

On Time Delivery

On Time Delivery In Full
Thank You!
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

- Survey
- CHAI
- Average

Survey: 5.7%, 4.7%, 5.3%, 5.7%, 5.8%, 6.0%, 6.3%, 6.5%, 6.7%
CHAI: 5.7%, 4.7%, 5.3%, 5.3%, 5.7%, 5.8%, 6.0%, 6.3%, 6.5%, 6.7%
Average: 5.2%, 4.7%, 5.3%, 5.6%, 5.8%, 6.0%, 6.3%, 6.5%, 6.7%
Historical and Projected Average Number on ART in LMIC based on Linear, Country target and Fast Track

<table>
<thead>
<tr>
<th>Year</th>
<th>Children, second line</th>
<th>Children, first line</th>
<th>Adult, second line</th>
<th>Adult, first line</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>62 000</td>
<td>880 000</td>
<td>1 140 000</td>
<td>18 000 000</td>
</tr>
<tr>
<td>2018</td>
<td>67 000</td>
<td>910 000</td>
<td>1 240 000</td>
<td>19 200 000</td>
</tr>
<tr>
<td>2019</td>
<td>75 000</td>
<td>980 000</td>
<td>1 430 000</td>
<td>21 800 000</td>
</tr>
<tr>
<td>2020</td>
<td>83 000</td>
<td>1 010 000</td>
<td>1 520 000</td>
<td>22 500 000</td>
</tr>
<tr>
<td>2021</td>
<td>90 000</td>
<td>1 020 000</td>
<td>1 610 000</td>
<td>23 200 000</td>
</tr>
<tr>
<td>2022</td>
<td>89 000</td>
<td>960 000</td>
<td>1 690 000</td>
<td>23 700 000</td>
</tr>
<tr>
<td>2023</td>
<td>92 000</td>
<td>920 000</td>
<td>1 780 000</td>
<td>24 100 000</td>
</tr>
</tbody>
</table>
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)

Survey

CHAI + MPP

ZDV
TDF
ABC
TAF

<table>
<thead>
<tr>
<th>Year</th>
<th>Survey</th>
<th>CHAI + MPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>69.5%</td>
<td>8%</td>
</tr>
<tr>
<td>2015</td>
<td>80.0%</td>
<td>0%</td>
</tr>
<tr>
<td>2016</td>
<td>79.5%</td>
<td>0%</td>
</tr>
<tr>
<td>2017</td>
<td>82.0%</td>
<td>1%</td>
</tr>
<tr>
<td>2018</td>
<td>85.5%</td>
<td>0.6%</td>
</tr>
<tr>
<td>2019</td>
<td>90.0%</td>
<td>0.6%</td>
</tr>
<tr>
<td>2020</td>
<td>92.0%</td>
<td>0.6%</td>
</tr>
<tr>
<td>2021</td>
<td>93%</td>
<td>0%</td>
</tr>
<tr>
<td>2022</td>
<td>88%</td>
<td>4%</td>
</tr>
<tr>
<td>2023</td>
<td>82%</td>
<td>1%</td>
</tr>
</tbody>
</table>
3TC and FTC Share of Adult Secondary NRTIs

Survey

CHAI + MPP

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%


3TC FTC

26.0% 24.0% 25.5% 21.0% 12.0% 10.5% 12.5% 15.5%

74.0% 76.0% 74.5% 79.0% 88.0% 89.5% 87.5% 84.5%
NNRTI and DTG Share of Adult market

Survey

NVP  EFV  DTG  CHAI + MPP

2016  83%  18%  0%
2017  82%  17%  2%
2018  77%  19%  8%
2019  69%  19%  9%
2020  48%  27%  6%
2021  47%  27%  4%
2022  39%  27%  2%
2023  30%  30%  1%
Adult Share of PIs

Note: assumes DRV-based therapy remains more expensive than LPV- or ATV-based therapy.
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)

Survey

Survey + GPRM + MPP

UNAIDS

World Health Organization

16
3TC and FTC Share of Paediatric Secondary NRTIs

- **Survey**
  - 99% in 2016
  - 99% in 2017
  - 99% in 2018
  - 99% in 2019
  - 99% in 2020
  - 98% in 2021
  - 98% in 2022
  - 98% in 2023

- **Survey + GPRM + MPP**
  - 1% in 2016
  - 1% in 2017
  - 1% in 2018
  - 1% in 2019
  - 1% in 2020
  - 1% in 2021
  - 2% in 2022
  - 2% in 2023

- **3TC**
  - 99% in 2016
  - 99% in 2017
  - 99% in 2018
  - 99% in 2019
  - 99% in 2020
  - 98% in 2021
  - 98% in 2022
  - 98% in 2023

- **FTC**
  - 1% in 2016
  - 1% in 2017
  - 1% in 2018
  - 1% in 2019
  - 1% in 2020
  - 1% in 2021
  - 2% in 2022
  - 2% in 2023
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)

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

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

Current (Simplified) FDA Review Process:

PEPFAR Application → FDA Review/Decision → TA’d/Approved ARVs posted on FDA’s public site

USAID and other entities procure ARVs

WHO uses some ARVs for their own list (not pre-qualified, no CRP)

Companies volunteer applications → CRP-Lite

Goals:
1) Reduce duplication of work
2) Faster pre-qualification
3) Faster in-country registration

Current (Simplified) WHO Pre-qualification and CRP Processes:

Application → Pre-qualification Review/Decision → Pre-qualified ARVs posted on WHO’s public site

Entities procure ARVs

CRP process to register in-country → In-country Registration
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.
“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.
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.
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);


- 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

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

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 new 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.”

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.

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
<table>
<thead>
<tr>
<th>Contract Area</th>
<th>Contract Type</th>
<th>Description</th>
<th>Awarding Parties</th>
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<tbody>
<tr>
<td>GHSC-Procurement and Supply Management (GHSC-PSM)</td>
<td>Single-award IDIQ</td>
<td>Procurement &amp; shipping of health commodities; supply chain technical assistance</td>
<td>Chemonics Int'l</td>
</tr>
<tr>
<td>GHSC-Quality Assurance (GHSC-QA)</td>
<td>Contract</td>
<td>Quality assurance of procured commodities; technical assistance</td>
<td>FHI360</td>
</tr>
<tr>
<td>GHSC-Business Intelligence and Analytics (GHSC-BIA)</td>
<td>Contract</td>
<td>Collect and integrate data across programs to support GHSC management and coordination</td>
<td>Intelicog</td>
</tr>
<tr>
<td>GHSC-Rapid Test Kits (GHSC-RTK)</td>
<td>Single-award IDIQ</td>
<td>Procurement &amp; shipping of HIV RTKs</td>
<td>Remote Medical Int'l</td>
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<tr>
<td>GHSC-Technical Assistance (GHSC-TA)</td>
<td>Multiple-award IDIQ</td>
<td>Supply chain technical assistance</td>
<td>Chemonics Int'l Axios LMI PWC</td>
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<tr>
<td>Medicines, Technologies, and Pharmaceutical Services (MTaPS)</td>
<td>Contract</td>
<td>Technical assistance for strengthening pharmaceutical systems</td>
<td>MSH</td>
</tr>
<tr>
<td>Promoting the Quality of Medicines (PQM+)</td>
<td>Cooperative Agreement</td>
<td>Technical assistance for medicines quality assurance mechanisms</td>
<td>USP</td>
</tr>
</tbody>
</table>
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
  o Active Ingredients
  o Strength
  o Dosage Form
  o Package Size
  o Shelf-life
  o Storage Conditions
  o Supplier
  o FPP Manufacturer
  o FPP Manufacturing Site(s)
  o Packaging Material
  o Regulatory Basis of Approval
  o US FDA Application Type and Number

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

- Product Information

  o Collected through GHSC-QA Abbreviated Technical Product Questionnaire

  o Manufacturer provided documentation through RFQ manufacturing campaigns
Product Eligibility Challenges

• Submission Challenges
  o No Submission
  
  o Incomplete Documentation

  o Submitted old technical questionnaires, without updates. Thus detailed product information and updates are not available.
Product Eligibility Challenges

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

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

• Summary
  o Risks identified are mostly related to FPP and API manufacturing site GMP inspections.
  o 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.
  o 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

Overview of Product Quality Incidents (LOP)
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

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

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

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

❖ **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

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
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

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

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

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

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

Needed: more extensive use of inexpensive starting materials

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

Needed: manufacturability in both batch and flow (lower capital costs, economies of scale at lower volumes)
M4ALL Approach:

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

M4ALL: Transforming Access To Both In Market and In Development Treatments
Our Building Blocks

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

Process Cost of Goods

\[ \sum \text{starting material costs} \times \sum \text{Yield} \]

Process Mass Intensity

\[ \text{PMI} = \frac{\text{mass of reactants}}{\text{mass of products}} \]
Environmental Policy Changes

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

**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

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

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

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:

2\textsuperscript{nd} 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: Full Roadmap**

1. **Novel Chemistry**
   - Commercial Process
   - Substitute lower cost raw materials
   - Simplify operations
   - Increase yields
   - Reduce solvent use and waste

2. **Transfer to API Manufacturers**
   - Transfer process to manufacturers
   - Substitute lower cost raw materials
   - Simplify operations
   - Increase yields
   - Reduce solvent use and waste

3. **Track Price Reductions**

---

**NEVIRAPINE PROGRESS**

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

**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

---

**NEVIRAPINE PRICE TRENDS (2014-2016)**

- Price decrease of 9% so far translates to estimated savings of approximately $7.8M in 2015 alone
Emtricitabine (FTC) Example

**Volume sale**: 120 MT/year

Common Route for FTC

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

\[
\begin{align*}
\text{2016} & : \text{16/kg} \\
\text{2018} & : \text{28/kg}
\end{align*}
\]

5-Fluorocytosine (5-FC)

\[
\begin{align*}
\text{2016} & : \text{32/kg} \\
\text{2018} & : \text{78/kg}
\end{align*}
\]

1. Toxic Reagents (HF, F\textsubscript{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

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%

Original Process Released Jan 2019
Updated Process Released Nov 2019
Emtricitabine (FTC) Price Tracking

- 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

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

Dolutegravir (DTG)

**Volume sale:** ~ 200 MT/year by 2020

**Common Route for DTG**
Dolutegravir Cost Drivers

Dolutegravir (DTG)
Volume sale: ~ 200 MT/year by 2020

Common Route for DTG
Dolutegravir Cost Drivers

MeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-Me

MeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-Me

MeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-Me

MeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-MeMeO-\(\text{C}=\text{O}\)-Me

Cabotegravir

Dolutegravir

Bictegravir

Continuous Preparation of 4-Pyridone

Telescop ed 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.

Step 1 Intermediate

Step 2 Intermediate

Released May 2019
M4ALL Preparation of (R)-3-aminobutanol

Isolated yield: 65-70%

Use of inexpensive starting materials:
- D-homo-β-alanine
- Sodium aluminum hydride
M4ALL Portfolio

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

Tuberculosis
- In Development Treatments

Malaria
- In Development Treatments
Summary

- 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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Anita Deshpande  
Market Engagement Director  
deshpandea2@vcu.edu

Perrer Tosso  
Global Innovation Manager  
pitosso@vcu.edu
2019 WHO guidelines and future perspectives on ARV optimization

Marco Vitoria, WHO HQ
Annual ARV Buyer Seller Summit
24-27 Nov 2019
## WHO ARV Guidelines Evolution: 2002 to 2019

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<tr>
<td>Why to start</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 350</td>
<td>CD4 ≤ 500</td>
<td>Treat All&lt;br&gt;- CD4 ≤ 350 as priority&lt;br&gt;- Programmatic focus on KPs</td>
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<tr>
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<td></td>
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<td>- consider 350&lt;br&gt;- TB at CD4 ≤ 350</td>
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<td></td>
<td></td>
<td>Treat All&lt;br&gt;- CD4 ≤ 350 as priority&lt;br&gt;- Programmatic focus on KPs</td>
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<td>1st Line ART</td>
<td>8 options&lt;br&gt;- AZT preferred</td>
<td>4 options&lt;br&gt;- AZT preferred</td>
<td>8 options&lt;br&gt;- AZT/TDF preferred&lt;br&gt;- d4T dose reduction</td>
<td>6 options (FDC)&lt;br&gt;- AZT/TDF preferred&lt;br&gt;- d4T phase out</td>
<td>1 preferred option (FDC)&lt;br&gt;- TDF/XTC/EFV preferred (all pops)&lt;br&gt;- transition to new alternative ARV options&lt;br&gt;(DTG, EFV)</td>
<td>1 preferred option (FDC)&lt;br&gt;- TDF/XTC/EFV preferred (all pops)&lt;br&gt;- transition to new alternative ARV options&lt;br&gt;(DTG, EFV)</td>
<td>1 preferred option (FDC)&lt;br&gt;- TDF/XTC/EFV preferred (all pops)&lt;br&gt;- transition to new alternative ARV options&lt;br&gt;(DTG, EFV)</td>
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<tr>
<td>2nd Line ART</td>
<td>No (Desirable)</td>
<td>No (Desirable)</td>
<td>Yes (Tertiary centers)</td>
<td>Yes (Phase in approach)</td>
<td>Yes (preferred for monitoring, use of PoC, DBS)</td>
<td>Yes (preferred for monitoring, scale up all technologies)&lt;br&gt;- CD4 monitoring can be stopped if patient virally supressed</td>
<td>DTG as preferred 2nd line option&lt;br&gt;(if not used in 1st line)</td>
</tr>
<tr>
<td>3rd Line ART</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>DRV/r, RAL, ETV</td>
<td>DRV/r, RAL, ETV</td>
<td>DRV/r, RAL, ETV, DTG</td>
<td>DRV/r, ETV, DTG</td>
</tr>
<tr>
<td>Viral Load Testing</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes (preferred for monitoring and can be used for switching decision from TLE to TLD in stable patients)</td>
</tr>
</tbody>
</table>

### Earlier initiation
- **1st Line ART**
  - Treat All<br>- CD4 ≤ 350 as priority<br>- Programmatic focus on KPs
- **2nd Line ART**
  - DTG as preferred 2nd line option<br>(if not used in 1st line)
- **3rd Line ART**
  - DRV/r, ETV, DTG

### Simpler treatment
- **1st Line ART**
  - 8 options<br>- AZT preferred
- **2nd Line ART**
  - Boosted and non-boosted PIs<br>- Heat stable co-formulation: ATV/r, LPV/r
- **3rd Line ART**
  - DRV/r, RAL, ETV

### Less toxic, more robust regimens
- **1st Line ART**
  - 6 options (FDC)<br>- AZT/TDF preferred<br>- d4T phase out
- **2nd Line ART**
  - Boosted PIs<br>- Heat stable co-formulation: ATV/r, LPV/r<br>- Heat stable co-formulation: ATV/r, LPV/r<br>- new alternative options<br>(DRV/r, LPV/r + RAL)
- **3rd Line ART**
  - DRV/r, RAL, ETV, DTG

### Better and simpler monitoring
- **1st Line ART**
  - 4 options<br>- AZT preferred<br>- TB at CD4 ≤ 350<br>- CD4 ≤ 350 as priority<br>- TB, HBV, PW, SDC at any CD4
- **2nd Line ART**
  - Boosted PIs<br>- Heat stable co-formulation: ATV/r, LPV/r<br>- Heat stable co-formulation: ATV/r, LPV/r<br>- new alternative options<br>(DRV/r, LPV/r + RAL)
- **3rd Line ART**
  - DRV/r, RAL, ETV, DTG

---

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus Load Testing</td>
<td>No</td>
<td>No</td>
<td>Yes (Tertiary centers)</td>
<td>Yes (Phase in approach)</td>
<td>Yes (preferred for monitoring, use of PoC, DBS)</td>
<td>Yes (preferred for monitoring, scale up all technologies)&lt;br&gt;- CD4 monitoring can be stopped if patient virally supressed</td>
<td>Yes (preferred for monitoring and can be used for switching decision from TLE to TLD in stable patients)</td>
</tr>
</tbody>
</table>
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)
## Optimization profiles of new ARV drugs in WHO guidelines comparative analysis

<table>
<thead>
<tr>
<th>Optimization criteria</th>
<th>DTG</th>
<th>EFV&lt;sub&gt;400&lt;/sub&gt;</th>
<th>TAF</th>
<th>DRV/r&lt;sub&gt;400/50&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy and safety</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Virologic potency</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Lower toxicity</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>High genetic barrier to resistance</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Simplification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Available as generic FDC</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Low pill burden/pill size</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Harmonization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use in pregnant women</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Use in childbearing age women</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Use in children</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Use in HIV-associated TB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Few drug interactions</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low price potential</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

* DRVr 400/100 OD has been studied.*
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)

For more details:

- [https://www.who.int/hiv/pub/arv/treat-all-uptake/en/](https://www.who.int/hiv/pub/arv/treat-all-uptake/en/)

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](https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf?ua=1)

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 2\textsuperscript{nd} and 3\textsuperscript{rd} line with DTG
## 2019 WHO ART Guidelines: What has been changed?

<table>
<thead>
<tr>
<th>Topic</th>
<th>2018 interim guidelines</th>
<th>2019 updates</th>
</tr>
</thead>
</table>
| **Use of DTG in 1\(^{\text{st}}\) 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 1\(^{\text{st}}\) 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**  
  - **Strong recommendation**  
  - Moderate certainty of evidence  
  - **EFV600 used in special situations**                                                                                                                                                                                                                                          |
| **Use of DTG in 2\(^{\text{nd}}\) line** | **DTG as preferred option if not used in 1\(^{\text{st}}\) 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 1\(^{\text{st}}\) 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 1\(^{\text{st}}\) line**  
  - **Strong recommendation**  
  - Moderate certainty of evidence |
PICO questions for 2019 update

DTG in 1\textsuperscript{st} 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?

DTG in 2\textsuperscript{nd} line
- 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?

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

- **SYSTEMATIC REVIEWS - NMA**
- **QUALITY OF EVIDENCE**
- **FEASIBILITY & COST**
- **VALUES & PREFERENCES**
- **2018 RECOMMENDATIONS**

**ETHICS**
- QUALITATIVE DATA REVIEWS
- COMMUNITY & HCW SURVEYS & CONSULTATIONS
- PROGRAMME MANAGERS SURVEY

**SYSTEMATIC REVIEWS - NMA**
- ARV TOXICITY REVIEWS
  - NTD, Weight Gain
  - MODELLING (CEPAC, Phillips, UCT)
  - SURVEY OF ARV (AMDS, GAM, Country DTG guidelines)
  - DRUG COSTING (GPRM, AMDS)

**QUALITY OF EVIDENCE**

**FEASIBILITY & COST**

**VALUES & PREFERENCES**

**2018 RECOMMENDATIONS**
## Safety and Efficacy of DTG and EFV_{600} in 1st line ART

### (summary 2019 WHO Sys Review & NMA)

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

### Efficacy outcomes

**Treatment discontinuation (any or due AEs)**: DTG is better with high quality of evidence.

**Viral suppression (4-96 weeks), viral suppression at delivery (PW), transmission (PW)**: DTG is probably better with high to moderate quality of evidence.

**CD4 recovery (24-144 weeks)**: DTG is probably better with high to moderate quality of evidence.

**Mortality**: Comparable with low quality of evidence.

**Neuropsychiatric AEs (any grade), depression (grade 3 or 4), dizziness (any grade)**: DTG is probably better with moderate to low quality of evidence.

**Sleep disorders (any grade)**: Comparable with very low quality of evidence.

**Body weight gain**: EFV is probably better with moderate quality of evidence.

**NTD**: EFV may be better with low quality of evidence.

**HIVDR (overall, NRTI or anchor drug)**: DTG is probably better with high to moderate quality of evidence.

### Resistance outcomes

Reference: Steve Kanters, For WHO ARV GDG, 5-7 June 2019
<table>
<thead>
<tr>
<th>major outcomes</th>
<th>EFV\textsubscript{400} vs EFV\textsubscript{600}</th>
<th>quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment discontinuation (due AEs)</td>
<td>EFV\textsubscript{400} better</td>
<td>high to moderate</td>
</tr>
<tr>
<td>Viral suppression (48-96 weeks), VL suppression if baseline &gt; 100,000 (48 weeks)</td>
<td>comparable</td>
<td>moderate</td>
</tr>
<tr>
<td>CD4 recovery (24-96 weeks)</td>
<td>comparable</td>
<td>moderate</td>
</tr>
<tr>
<td>Mortality</td>
<td>comparable</td>
<td>low</td>
</tr>
<tr>
<td>Neuropsychiatric AEs (any grade), depression (grade 3 or 4), dizziness (any grade), sleep disorders (any grade)</td>
<td>comparable</td>
<td>low to very low</td>
</tr>
<tr>
<td>Body weight gain</td>
<td>comparable</td>
<td>low</td>
</tr>
<tr>
<td>Treatment related adverse events</td>
<td>EFV\textsubscript{400} better</td>
<td>moderate</td>
</tr>
<tr>
<td>HIVDR (overall, NRTI or anchor drug)</td>
<td>comparable</td>
<td>very low</td>
</tr>
</tbody>
</table>

Reference: Steve Kanters, For WHO ARV GDG, 5-7 June 2019
### 2019 WHO recommendations: First-line ART regimens

#### Table 1. Preferred and alternative first-line ART regimens

<table>
<thead>
<tr>
<th>Population</th>
<th>Preferred first-line regimen</th>
<th>Alternative first-line regimen</th>
<th>Special circumstances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents</td>
<td>TDF + 3TC (or FTC) + DTG*</td>
<td>TDF + 3TC + EFV 400 mg*</td>
<td>TDF + 3TC (or FTC) + EFV 600 mg*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AZT + 3TC + EFV 600 mg*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TDF + 3TC (or FTC) + PI/r*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TDF + 3TC (or FTC) + RAL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TAF + 3TC (or FTC) + DTG</td>
</tr>
<tr>
<td></td>
<td>ABC + 3TC + DTG*</td>
<td>ABC + 3TC + LPV/r</td>
<td>ABC + 3TC + EFV (or NVP)</td>
</tr>
<tr>
<td></td>
<td>ABC + 3TC + RAL*</td>
<td>ABC + 3TC + LPV/r</td>
<td>AZT + 3TC + NFV (or NVP)</td>
</tr>
<tr>
<td></td>
<td>TAF + 3TC (or FTC) + DTG*</td>
<td></td>
<td>AZT + 3TC + LPV/r (or RAL)</td>
</tr>
<tr>
<td>Neonates</td>
<td>AZT + 3TC + RAL*</td>
<td>AZT + 3TC + NVP</td>
<td>AZT + 3TC + LPV/r*</td>
</tr>
</tbody>
</table>

---

*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.
*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 a woman identifies pregnancy after the first trimester, DTG should be initiated or continued for the duration of the pregnancy (Box 2).
*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.
*TAF may be considered for people with established osteoporosis and/or impaired kidney function.

*For age and weight groups with approved DTG dosing.
*RAL should be used as an alternative regimen only if LPV/r solid formulations are not available.
*For age and weight groups with approved TAF dosing.
*EFV should not be used for children younger than three years of age.
*Neonates starting ART with an RAL-based regimen should transition to an LPV/r solid formulation as soon as possible.
*LPV/r syrup or granules can be used if starting after two weeks of age.
**Tsepmo: Prevalence of NTDs by ARV Exposure**

- **Conception**
  - DTG (n = 1683)
    - Total NTDs: 5/1683
    - Prevalence difference, % (95% CI): Ref
  - Non-DTG (n = 14,792)
    - Total NTDs: 15/14,792
    - Prevalence difference, % (95% CI): 0.20 (0.01-0.59)
  - EFV (n = 7,959)
    - Total NTDs: 3/7,959
    - Prevalence difference, % (95% CI): 0.26 (0.07-0.66)

- **Pregnancy**
  - DTG (n = 3,840)
    - Total NTDs: 1/3,840
    - Prevalence difference, % (95% CI): 0.27 (0.06-0.67)
  - HIV Negative (n = 89,372)
    - Total NTDs: 70/89,372
    - Prevalence difference, % (95% CI): 0.22 (0.05-0.62)

- **NTDs per exposures since May 2018, n/N**
  - DTG: 1/1275
  - Non-DTG: 1/3492
  - EFV: 0/2172
  - HIV Negative: 1/1028

**Different phenotypes of neural tube defects**

---

Zash. IAS 2019. Abstr MOAX0105LB.
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.
Risk vs Benefits of DTG in Women of Childbearing-Potential at a Population Level


**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**

- “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 contraception vs EFV only**

- “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*
Folate Food Fortification and NTD risk

Fortification begun

USA

36% decline

66% decline

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

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

Williams, MMWR, 2015

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

36 countries

- All WCBP non-DTG based regimen 
  - 3 countries
    - Burundi, Gabon, Equatorial Guinea

- WCBP can access DTG if on Contraception
  - 25 countries
    - ANY contraception 
      - 2 countries
        - Cameroon, Ukraine
    - Long Acting Contraception 
      - 15 countries
        - Botswana, Brazil, CAR, Chad, Congo, Cote d’Ivoire, DRC, Gabon, Kenya, Haiti, Mozambique, Nigeria, Sao Tome & Principe, South Africa, Venezuela
    - Consistent reliable contraception 
      - 8 countries
        - Argentina, Burkina Faso, Ethiopia, Ghana, Niger, Senegal, Syria, Togo

- Informed choice
  - 8 countries
    - Eswatini, Lesotho, Malawi, Tanzania, Rwanda, Uganda, Zambia, Zimbabwe
## Safety and Efficacy of DTG and PIs (LPVr) in 2\(^{nd}\) line ART
(s Summary 2019 WHO Sys Review & NMA)

<table>
<thead>
<tr>
<th>major outcomes</th>
<th>DTG vs LPVr</th>
<th>quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral suppression (4-96 weeks)</td>
<td><strong>DTG better</strong></td>
<td>high</td>
</tr>
<tr>
<td>Viral suppression baseline VL &gt; 100,000 (48 weeks)</td>
<td>comparable</td>
<td>moderate</td>
</tr>
<tr>
<td>CD4 recovery (24-48 weeks)</td>
<td>comparable</td>
<td>moderate</td>
</tr>
<tr>
<td>Mortality</td>
<td>comparable</td>
<td>low</td>
</tr>
<tr>
<td>Neuropsychiatric AEs (any grade)</td>
<td>comparable</td>
<td>low</td>
</tr>
<tr>
<td>Treatment related SAE</td>
<td>comparable</td>
<td>low</td>
</tr>
<tr>
<td>Treatment emergent AE, related AEs</td>
<td><strong>DTG probably better</strong></td>
<td>high</td>
</tr>
<tr>
<td>Treatment discontinuation (any or due AEs)</td>
<td><strong>DTG probably better</strong></td>
<td>high</td>
</tr>
<tr>
<td>HIVDR (overall)</td>
<td>comparable</td>
<td>very low</td>
</tr>
</tbody>
</table>

Reference: Steve Kanters, For WHO ARV GDG, 5-7 June 2019
2019 WHO recommendations: Second-line ART regimens

Table 2. Preferred and alternative second-line ART regimens

<table>
<thead>
<tr>
<th>Population</th>
<th>Failing first-line regimen</th>
<th>Preferred second-line regimen</th>
<th>Alternative second-line regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents³</td>
<td>TDF + 3TC (or FTC) + EFV (or NVP)</td>
<td>AZT + 3TC + ATV/r (or LPV/r)³</td>
<td>AZT + 3TC + DRV/r³</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC (or FTC) + EFV (or NVP)</td>
<td>AZT + 3TC + DTG³</td>
<td>AZT + 3TC + ATV/r (or LPV/r or DRV/r)³</td>
</tr>
<tr>
<td>Children and infants</td>
<td>ABC + 3TC + DTG³</td>
<td>AZT + 3TC + ATV/r (or LPV/r)³</td>
<td>AZT + 3TC + DRV/r³</td>
</tr>
<tr>
<td></td>
<td>ABC (or AZT) + 3TC + LPV/r</td>
<td>AZT + 3TC + ATV/r (or LPV/r)³</td>
<td>AZT + 3TC + RAL</td>
</tr>
<tr>
<td></td>
<td>ABC (or AZT) + 3TC + LPV/r</td>
<td>AZT + 3TC + ATV/r (or LPV/r)³</td>
<td>AZT (or ABC) + 3TC + RAL</td>
</tr>
<tr>
<td></td>
<td>ABC (or AZT) + 3TC + EFV</td>
<td>AZT (or ABC) + 3TC + DTG³</td>
<td>AZT (or ABC) + 3TC + LPV/r (or ATV/r)³</td>
</tr>
<tr>
<td></td>
<td>ABC (or AZT) + 3TC + EFV</td>
<td>AZT (or ABC) + 3TC + DTG³</td>
<td>AZT (or ABC) + 3TC + LPV/r (or ATV/r)³</td>
</tr>
<tr>
<td></td>
<td>ABC + 3TC + NVP</td>
<td>ABC + 3TC + DTG³</td>
<td>ABC + 3TC + LPV/r (or ATV/r or DRV/r)³</td>
</tr>
</tbody>
</table>

³Sequencing of PIIs are used in first-line ART: ATV/r or LPV/r depending on programmatic considerations) + TDF + 3TC (or FTC) and then AZT + 3TC + DTG in second-line ART.

³³Effective 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).

³³³TAF (tenofovir alafenamide) can be used as an alternative NRTI in special situations for adults and adolescents.

³³³³RAL + LPV/r can be used as an alternative second-line ART regimen for adults and adolescents.

³³³³³The 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 NRTIs 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.

³³³³³³³ATV/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.

³³³³³³³³ID/RV should not be used for children younger than three years and should be combined with appropriate dosing of ritonavir.
## TLD transition at a glance

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

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
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 groups for weight gain analysis
  - HIV+ women starting DTG btn conception and 17 wk GA (1st ANC wt 65.6 kg)
  - HIV+ women starting EFV btn conception and 17 wk GA (1st ANC wt 65.7 kg)
  - HIV-uninfected women of similar age, presenting for ANC <17 wk (1st ANC wt 66.5 kg)

Adjusted Mean Difference Weight Gain 18-36 wk (kg)
Adjusted Mean Difference Weekly Weight Gain (kg/wk)
→ 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

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

New indicators for toxicity in case surveillance & routine monitoring

WHO global databases

Central registry for drug safety in pregnancy

Generic DTG ADR notification form

Toolkit with PV module for children

Pregnancy & birth defect registry tools

WHO global ARV toxicity monitoring database

South Africa

UNITAID partnership

WHO / TDR central database for safety evaluation of DTG

Botswana

Kenya

MOH and IAPD

Brazil

MOH

Training

South Africa

South Africa

WHO / TDR Global registry for Drug Safety in Pregnancy

Malawi

WHO / TDR Global registry for Drug Safety in Pregnancy

Botswana

WHO / TDR Global registry for Drug Safety in Pregnancy

Malawi

Pregnant women

General population inc. children & adolescents
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

*ARV toxicity monitoring approaches

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 introduced to monitor ADRs to DTG, GAM 2019 data**

- 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 approaches:

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

# Main drug-drug interactions with DTG

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

* 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.
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**

**Operational / Service Delivery GDG Meeting Sept 2020**

**Launch Full 2020 Consolidated HIV Guidelines Dec 1 2020**

**Community V&P Work**
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

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

**Short-term**
1-2 years
- TDF/XTC/DTG
- TDF/3TC/EFV<sub>400</sub>
- 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 considered if new data become available in the future (bictegravir, doreavirine, DTG/3TC, DRVr/3TC, DTG/DRV/r)
§ Low dose standard formulation (400/100mg) or standard dose nanoformulation (800/100mg)

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

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

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

All members Guidelines Development Group members
• Elaine Abrams & Serge Eholie
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• Francoise Renaud
• Nathan Ford
• Silvia Bertagnolio
• Lara Vojnov

• Vindi Singh
• Morkor Newman
• Serena Brusamento
• Chantal Migone

• Ajay Rangaraj
• Anisa Ghadrshenasa

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• AFROCAB, iBASE, ITPC, Salamander Trust, ICW, GPN+, APN+
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 appraisal 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

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin Auton</td>
<td>Global Fund</td>
</tr>
<tr>
<td>Meg Doherty</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>

#### Experts Providing Recommendations

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jacqueline Wambui</td>
<td>Health Gap / National Empowerment Network of People Living with HIV/AIDS in Kenya (NEPHAK)</td>
</tr>
<tr>
<td>George Siberry</td>
<td>USAID</td>
</tr>
<tr>
<td>Luckyboy Mkhnondwane</td>
<td>Treatment Action Campaign</td>
</tr>
<tr>
<td>Francoise Renaud</td>
<td>World Health Organization</td>
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<tr>
<td>Marco Vitoria</td>
<td>World Health Organization</td>
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<td>Nathan Ford</td>
<td>World Health Organization</td>
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<td>Martina Penazzato</td>
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<tr>
<td>Polly Clayden</td>
<td>HIV i-Base</td>
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<tr>
<td>Andrew Hill</td>
<td>University of Liverpool</td>
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#### ART Optimization Program FUNDING Agencies

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Katherine Blumer</td>
<td>Unitaid</td>
</tr>
<tr>
<td>Danielle Ferris</td>
<td>Unitaid</td>
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<tr>
<td>Carmen Perez Casas</td>
<td>Unitaid</td>
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<td>Denitza Andjelic</td>
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<td>Tim Ryan</td>
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<tr>
<td>Emily Harris</td>
<td>USAID</td>
</tr>
<tr>
<td>Mesai Belayneh</td>
<td>USAID / Supply Chain</td>
</tr>
<tr>
<td>Mary Catharine McKeithen</td>
<td>USAID</td>
</tr>
<tr>
<td>Julia Martin</td>
<td>USG/State Department</td>
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#### Implementer Organizations

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Caroline Middlecote</td>
<td>Clinton Health Access Initiative</td>
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<td>Polly Clayden</td>
<td>HIV i-Base</td>
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<tr>
<td>Eric Delaporte</td>
<td>IRD</td>
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<tr>
<td>Nicola Loffredi</td>
<td>Medicines Patent Pool</td>
</tr>
<tr>
<td>Hannah Moak</td>
<td>Medicines Patent Pool</td>
</tr>
<tr>
<td>Sandra Nobre</td>
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</tr>
<tr>
<td>Michelle Moorhouse</td>
<td>Wits RHI - Ezintsha</td>
</tr>
<tr>
<td>Saye Khoo</td>
<td>University of Liverpool</td>
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<td>Andrew Hill</td>
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<tr>
<td>Mark Polizzotto</td>
<td>University of New South Wales</td>
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<tr>
<td>Isabelle Andrieux- Meyer</td>
<td>DNDi</td>
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<tr>
<td>Celia Serenata</td>
<td>Wits THI</td>
</tr>
<tr>
<td>Maureen Syowai</td>
<td>ICAP at Columbia University</td>
</tr>
<tr>
<td>Jen Cohn</td>
<td>EAGPAF</td>
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<td>AFRICOS</td>
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<tr>
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<tr>
<td>Eugene Choi</td>
<td>Medicines for All Institute</td>
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<td>Tim Cressey</td>
<td>Stellenbosch University</td>
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<td>Helen Rabie</td>
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<tr>
<td>Hiwot Haile-Selassie</td>
<td>WHO</td>
</tr>
<tr>
<td>Imelda Mahaka</td>
<td>PZAT</td>
</tr>
<tr>
<td>Annette Reinisch</td>
<td>Global Fund</td>
</tr>
<tr>
<td>Jinkou Zhao</td>
<td>Global Fund</td>
</tr>
<tr>
<td>Pablo Rojo</td>
<td>PENTA</td>
</tr>
<tr>
<td>Kenly Sikwese</td>
<td>AfroCAB</td>
</tr>
</tbody>
</table>
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

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

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 communities
**CADO 3 LIST**

**DRV/r**<sub>400/50</sub>: heat stable boosted formulation to optimize PI options in 2<sup>nd</sup> line (pill size)

**EFV<sub>400</sub>/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).
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

<table>
<thead>
<tr>
<th>Potential priority</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accelerate TLD transition</strong></td>
<td>• Long term safety (NTD and emerging AEs)</td>
</tr>
<tr>
<td></td>
<td>• Transition in stable patients (including those in 2nd line?)</td>
</tr>
<tr>
<td></td>
<td>• Robustness in real life conditions and NRTI resistance (genetic barrier)</td>
</tr>
<tr>
<td></td>
<td>• Support to transition plans</td>
</tr>
<tr>
<td><strong>Role of alternative regimens/drugs (TLE, PIs)</strong></td>
<td>• How to guarantee adequate supply chain /availability</td>
</tr>
<tr>
<td><strong>Accelerate the phase out of suboptimal drugs (eg: NVP)</strong></td>
<td>• Remove from next EML ?</td>
</tr>
<tr>
<td></td>
<td>• Support to phase out plans</td>
</tr>
<tr>
<td><strong>Improve access to DRV</strong></td>
<td>• Dose reduction and better formulations (FDCs, nanomedicines)</td>
</tr>
<tr>
<td></td>
<td>• High cost is also an important barrier</td>
</tr>
<tr>
<td></td>
<td>• Better promote it in 2nd line or reserve for 3rd line?</td>
</tr>
<tr>
<td><strong>Role of TAF (should replace TDF?)</strong></td>
<td>• Long term safety (body weight gain and emerging AEs)</td>
</tr>
<tr>
<td></td>
<td>• TB/HIV - is dose adjustment a solution?</td>
</tr>
<tr>
<td></td>
<td>• Transition in stable patients (all or only high risk groups?)</td>
</tr>
<tr>
<td></td>
<td>• Include in EoI ???</td>
</tr>
<tr>
<td><strong>Dual therapy (including long acting drugs and emerging classes)</strong></td>
<td>• What are the options in short, medium and long term?</td>
</tr>
<tr>
<td></td>
<td>• Can we go beyond than simplification strategy?</td>
</tr>
<tr>
<td></td>
<td>• Limited data on long term safety</td>
</tr>
</tbody>
</table>
PADO4: expanding the scope to address the full life-cycle and its specificities
<table>
<thead>
<tr>
<th>Status of Studies</th>
<th>Phase I</th>
<th>Phase IIa</th>
<th>Phase IIb</th>
<th>Phase III</th>
<th>Phase IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Pregnant</td>
<td>Pharmacokinetics, safety, tolerability</td>
<td>Pharmacodynamics, dose range</td>
<td>Definitive dose, efficacy</td>
<td>Efficacy, comparison to standard of care</td>
<td>Post-market approval surveillance, safety, rare events</td>
</tr>
<tr>
<td>Pregnant, Current Status of Studies</td>
<td>Not included</td>
<td>Not included</td>
<td>Not included</td>
<td>Generally not included; if woman becomes pregnant, stops drug, often comes off study</td>
<td>Phase I pregnancy study may or may not be done; post-market safety surveillance may or may not be done</td>
</tr>
<tr>
<td>Pregnant, Proposed Status of Studies</td>
<td>Not included</td>
<td>Not included</td>
<td>Phase I in parallel to phase IIb in pregnant women with limited options and hence favorable benefit/risk</td>
<td>If phase I during phase IIb, enroll into phase III trials</td>
<td>If phase I not done and drug will be used in pregnancy, do phase I</td>
</tr>
<tr>
<td></td>
<td>→exception: life-threatening conditions with no treatment available (e.g., Ebola)</td>
<td>→exception: life-threatening conditions with no treatment available (e.g., Ebola)</td>
<td></td>
<td>If phase I not done, phase I in parallel to or as substudy of phase III</td>
<td>If have phase I data, potential comparison to standard regimen used in pregnancy (safety)</td>
</tr>
</tbody>
</table>
Introducing DTG for children and adolescents

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.

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

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.
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 1\textsuperscript{st} and 2\textsuperscript{nd} line DTG ART vs standard of care in 700 HIV-infected children <18 years (recruiting add 80 children <14 kg)

<table>
<thead>
<tr>
<th>WHO Weight bands, kg</th>
<th>DTG DT* once daily (# tablets, daily dose, mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 to &lt;6 (&lt;6 months old)</td>
<td>2 (10mg)</td>
</tr>
<tr>
<td>3 to &lt;6 (&gt;6 months old)</td>
<td>2 (10mg)</td>
</tr>
<tr>
<td>6 to &lt;10</td>
<td>3 (15mg)</td>
</tr>
<tr>
<td>10 to &lt;14</td>
<td>4 (20mg)</td>
</tr>
<tr>
<td>14 to &lt;20</td>
<td>5 (25mg)</td>
</tr>
<tr>
<td>20 to &lt;25</td>
<td>6 (30mg)</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>WHO weight band</th>
<th>ODYSSSEY Weight Bands</th>
<th>Reference adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose mg/formulation</td>
<td>6&lt;10</td>
<td>10&lt;14</td>
</tr>
<tr>
<td>N</td>
<td>15 DT</td>
<td>20 DT</td>
</tr>
<tr>
<td>Dose/weight (range) mg/kg</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>( C_{\text{trough}} ) (CV%) mg/L</td>
<td>1.8 (15-2.2)</td>
<td>1.8 (1.6-2.0)</td>
</tr>
<tr>
<td>( AUC_{0-24h} ) (CV%) mg*h/L</td>
<td>49.3 (77)</td>
<td>77.0 (22)</td>
</tr>
<tr>
<td>( C_{\text{max}} ) (CV%) mg/L</td>
<td>5.4 (50)</td>
<td>8.0 (22)</td>
</tr>
</tbody>
</table>

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

- \( C_{\text{trough}} \) low in 6-<10kg weight band
- \( AUC \) inbetween adult QD and BID
- \( C_{\text{max}} \) somewhat higher than adult in higher weight bands (10~20)
How is the Ped ARV landscape expected to change?

**2018**

- Increased capacity for LPV/r pellets/granules

**2019**

- Facilitated intro of RAL granules for infected neonates
- Implementation guidance, tools and resources will be available for countries implementing birth testing

**2020**

- Supply is less of a constraint

**2021**

- Availability in country

---

- **DTG 50mg and TLD already available**
- **ABC/3TC/LPV/r “4 in 1”**
- **All P1093 cohorts (4 wks and up)**
- **DTG 5mg disp tablet**
- **DTG 10mg scored disp tab**

**FILED**

- SRA Approval ~ 6 mos
- Availability in country

**Anticipated filing**

- SRA Approval ~ 6 mos
- Availability in country
# PADO list evolution

<table>
<thead>
<tr>
<th>PADO 1-2013</th>
<th>PADO 2-2014</th>
<th>PADO 3-2016</th>
<th>PADO 4-2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPVr 4-in-1</td>
<td>LPVr 4-in-1 (30/15/40/10 mg)*</td>
<td>In advanced development</td>
<td></td>
</tr>
<tr>
<td>ABC/3TC/EFV</td>
<td>ABC/3TC/EFV (150/75/150 mg)*</td>
<td>In advanced development</td>
<td></td>
</tr>
<tr>
<td>ATVr</td>
<td>ATVr (100/33mg)*</td>
<td>Removed$</td>
<td></td>
</tr>
<tr>
<td>NVP 20 mg</td>
<td>NVP/AZT</td>
<td>NVP/AZT</td>
<td>Removed</td>
</tr>
<tr>
<td>RAL</td>
<td>RAL</td>
<td>RAL (50 mg scored)*</td>
<td>Removed</td>
</tr>
<tr>
<td>DRVr</td>
<td>DRVr</td>
<td>DRVr (120/20 mg)*</td>
<td>DRVr (120/20 mg)</td>
</tr>
<tr>
<td>DTG single</td>
<td>DTG paeds single</td>
<td>DTG paeds single (5 mg)*</td>
<td>DTG paeds single (10 mg scored) dispers tab</td>
</tr>
<tr>
<td>DTG/3TC/ABC</td>
<td>DTG/3TC/ABC</td>
<td>DTG/3TC/ABC (5/30/60 mg)*</td>
<td>DTG/3TC/ABC (5/30/60 mg) dispersible tab</td>
</tr>
<tr>
<td>F/TAF</td>
<td>F/TAF</td>
<td>F/TAF</td>
<td>XTC/TAF dispersible tablets</td>
</tr>
<tr>
<td>DTG/XTC/TAF</td>
<td>DTG/XTC/TAF</td>
<td>DTG/XTC/TAF</td>
<td>DTG/XTC/TAF dispersible tablets</td>
</tr>
<tr>
<td>DTG/DRVr</td>
<td>DTG/3TC</td>
<td>Removed</td>
<td></td>
</tr>
<tr>
<td>LA</td>
<td>bNab</td>
<td>MK 8591</td>
<td>Doravirine</td>
</tr>
<tr>
<td>bNab</td>
<td></td>
<td></td>
<td>New delivery technologies</td>
</tr>
</tbody>
</table>
### Summary of gaps and the trials/studies to answer them

<table>
<thead>
<tr>
<th>Questions /Side Effects /ADRs</th>
<th>Current Trial Data</th>
<th>Results from extended or new trials to help answer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NTD</strong>&lt;br&gt;- Longer term outcomes</td>
<td>TSEPAMO, APR, Enhanced Toxicity Monitoring</td>
<td>TSEPAMO Active Surveillance, Kenya, Uganda, Brazil, Malawi, S Africa</td>
</tr>
<tr>
<td><strong>Weight gain</strong>&lt;br&gt;- Role DTG /INSTI&lt;br&gt;- Role of TAF&lt;br&gt;- Background obesity rates</td>
<td>ADVANCE, Namsal, Vital records</td>
<td>ADVANCE, NAMSAL, ViIV, Gilead, Expanded active surveillance</td>
</tr>
<tr>
<td><strong>Hyperglycemia</strong>&lt;br&gt;- Role of DTG&lt;br&gt;- Role of other ARVs</td>
<td>No RCT, Uganda case series</td>
<td>ADVANCE, NAMSAL, DAWNING, DEFT, NIH Study</td>
</tr>
<tr>
<td><strong>Erectile Dysfunction</strong></td>
<td>No Data in 2019</td>
<td>As above</td>
</tr>
<tr>
<td><strong>Switching to DTG when stable on EFV</strong></td>
<td>No data in 2019</td>
<td>DEFT, Observe TLD</td>
</tr>
</tbody>
</table>
Trials Underway to Evaluate 6-month Multi-Month Dispensing (MMD)

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

Malawi & Zambia

Trials

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 Fatti1, Nicoletta Ngorima-Mahhena2, Frank Chirowa3, Benson Chiwaa2, Kudakwashe Takarinda3,4, Taurayi A. Tafuma2, Nyakadzo Mahachi2, Rudo Chikodzi5, Simon Nyadundu1, Charles A. Ayaji6, Tsitsi Mutusa-Adipo1,5, Owen Muquuru2, Euse Mofihlile1, Risa M. Hoffman1,7, and Ashraf Grimwood1,7

South Africa

Trials

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

Risa Hoffman1,7, Ashley Bardon1,2, Sydney Rosen3,4, Matthew Fox2,9, Thoko Kalia3, Thembi Xulu2, Angela Taylor3, and Ian Sanne2,9

BMC Public Health

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

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!
FY’ 19 Results

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

<table>
<thead>
<tr>
<th>INDICATOR</th>
<th>CUMULATIVE RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX_CURR</td>
<td>15,667,099</td>
</tr>
</tbody>
</table>
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 THEMIBISA (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

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 1\textsuperscript{st} line ART regimens

<table>
<thead>
<tr>
<th>First-line ART regimens\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>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</td>
</tr>
<tr>
<td>• Adults and adolescents\textsuperscript{b} (strong recommendation, moderate-certainty evidence)</td>
</tr>
<tr>
<td>• Infants and children with approved DTG dosing (conditional recommendation, low-certainty evidence)</td>
</tr>
<tr>
<td>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\textsuperscript{c} (strong recommendation, moderate-certainty evidence)</td>
</tr>
<tr>
<td>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)</td>
</tr>
<tr>
<td>4. A RAL-based regimen may be recommended as the preferred first-line regimen for neonates (conditional recommendation, very-low-certainty evidence)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Eligible Pediatric Population</th>
<th>LPV/r Oral Pellets*</th>
<th>LPV/r Oral Granules*</th>
<th>RAL Granules for Oral Suspension</th>
<th>RAL Chewable Tablets</th>
<th>DRV Tablet (with RTV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Age: 3+ months, and 2) Unable to fully swallow intact LPV/r pediatric tablet</td>
<td>1) Age: 2+ weeks, and 2) Unable to fully swallow intact LPV/r pediatric tablet</td>
<td>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.</td>
<td>To only serve as a temporary bridge for the shortest time possible between RAL granules and LPV/r solid formulation</td>
<td>CLHIV (≥3yo) failing a PI-based regimen</td>
<td></td>
</tr>
<tr>
<td>PEPFAR Preferred Formulation</td>
<td>40 mg/10 mg capsule</td>
<td>40 mg/10mg sachet</td>
<td>100 mg sachet</td>
<td>25 mg (can be chewed, crushed or dispersed for administration)</td>
<td>DRV 75 mg tablet (with RTV 25** mg or RTV 100 mg tablet – cannot be crushed)</td>
</tr>
</tbody>
</table>

*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

- LPVr 40/10 formulations
- LPVr/ABC/3TC, 4 in 1
- Ped ABC/3TC/DTG
- DRVr 120/20?

ANTICIPATED TIMELINE OF PRODUCT AVAILABILITY FOR PROUCREMENT
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
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
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**

**ARV Procurement Working Group (APWG)**
*Umbrella body supporting coordinated efforts to ensure timely and consistent access to ARVs*
- Guides the direction of the Procurement Consortium
- Advocates broadly for improved product selection/optimization
- Coordinates and collaborates with similar groups and governments
- Raises awareness with stakeholders on general and specific challenges in the ARV marketplace

**Market Coordination & Support**
- Collect, analyze, and disseminate market intelligence
- Provide country technical assistance for procurement and forecasting
- Support coordination of global stakeholders

**Procurement Consortium (PC)**
*Subgroup of transactional procurement agents focusing on alignment and coordination of procurement activities*
- Engages with suppliers
- Aligns member forecasts and forecasting
- Pools demand/coordinates ordering
- Ensures a competitive and transparent order allocation process amongst quality assured, eligible suppliers
- Facilitates procurement of high supply-risk, low volume formulations through Global Fund’s Rapid Supply Mechanism
- Monitors country market-related challenges
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
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
<table>
<thead>
<tr>
<th>Formula</th>
<th>Quantity</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/3TC (120/60 mg) Tablet (Disp) - 30</td>
<td>4,200,000</td>
<td>41%</td>
</tr>
<tr>
<td>LPV/r (100/25 mg) Tablet (HS) - 60</td>
<td>1,700,000</td>
<td>16%</td>
</tr>
<tr>
<td>ABC/3TC (120/60 mg) Tablet (Disp) - 60</td>
<td>1,300,000</td>
<td>13%</td>
</tr>
<tr>
<td>NVP (50 mg/5 ml) Oral Solution - 100ml</td>
<td>895,000</td>
<td>9%</td>
</tr>
<tr>
<td>AZT/3TC (60/30 mg) Tablet (Disp) - 60</td>
<td>890,000</td>
<td>9%</td>
</tr>
<tr>
<td>LPV/r (40/10 mg) Oral Pellet - HS - 120</td>
<td>640,000</td>
<td>6%</td>
</tr>
<tr>
<td>LPV/r (40/10 mg) Oral Granule - HS - 120</td>
<td>240,000</td>
<td>2%</td>
</tr>
</tbody>
</table>

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

### Non-Essential Formulations
<table>
<thead>
<tr>
<th>Formula</th>
<th>Quantity</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/3TC (60/30 mg) Tablet (Disp) - 60</td>
<td>1,700,000</td>
<td>73%</td>
</tr>
<tr>
<td>AZT (50 mg/5 ml) Oral Solution - 240ml</td>
<td>400,000</td>
<td>16%</td>
</tr>
<tr>
<td>NVP (50 mg/5 ml) Oral Solution - 240ml</td>
<td>135,000</td>
<td>6%</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>In-country delivery quarter</th>
<th>Lopinavir/Ritonavir 40mg/10mg, Pellets, 120 capsules</th>
<th>Lopinavir/Ritonavir 40mg/10mg, Oral Granules, 120 sachets</th>
<th>Lopinavir/Ritonavir 100mg/25mg, Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 2020</td>
<td><img src="image1" alt="Green Traffic Light" /></td>
<td><img src="image2" alt="Green Traffic Light" /></td>
<td><img src="image3" alt="Red Traffic Light" /></td>
</tr>
<tr>
<td>Q2 2020</td>
<td><img src="image1" alt="Green Traffic Light" /></td>
<td><img src="image2" alt="Green Traffic Light" /></td>
<td><img src="image4" alt="Orange Traffic Light" /></td>
</tr>
<tr>
<td>Q3 2020</td>
<td><img src="image1" alt="Green Traffic Light" /></td>
<td><img src="image2" alt="Green Traffic Light" /></td>
<td><img src="image5" alt="Green Traffic Light" /></td>
</tr>
<tr>
<td>Q4 2020</td>
<td><img src="image1" alt="Green Traffic Light" /></td>
<td><img src="image2" alt="Green Traffic Light" /></td>
<td><img src="image6" alt="Green Traffic Light" /></td>
</tr>
<tr>
<td>Q1 2021</td>
<td><img src="image1" alt="Green Traffic Light" /></td>
<td><img src="image2" alt="Green Traffic Light" /></td>
<td><img src="image7" alt="Green Traffic Light" /></td>
</tr>
<tr>
<td>Q2 2021</td>
<td><img src="image1" alt="Green Traffic Light" /></td>
<td><img src="image2" alt="Green Traffic Light" /></td>
<td><img src="image8" alt="Green Traffic Light" /></td>
</tr>
</tbody>
</table>

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

Check back often as new documents are released.

The APWG website includes relevant optimization documents
https://www.arvprocurementworkinggroup.org/home

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

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

November 2019
Washington, DC
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

- PEPFAR
- Kenya
- Republic of South Africa
- Global Fund

- Burkina Faso
- Cameroon
- Cote d’Ivoire
- Congo DRC
- Ethiopia
- Ghana
- Kenya
- Malawi
- Mozambique
- Nigeria
- South Africa
- Tanzania
- Uganda
- Zambia
- Zimbabwe

- TLD 30 tabs
- TLD 90 tabs
- TLD 180 tabs
- DTG 50
- TLE 600
- TLE 400 30 tabs
- TLE 400 90 tabs
- TEE
- ABC/3TC 600/300
- EFV 600
- 3TC/AZT 150/300
- TDF/3TC 300/300
- ABC/3TC 120/60
- ATV/r 300/100
- LPV/r 200/50
- LPV/r 100/25
- LPV/r 40/10 capsules/granules
- NVP oral 100ml suspension

58
13
5
17
23
Q4 2019

61
15
7
22
18
Q1 2020

52
9
3
22
17
Q2 2020

49
9
2
23
15
Q3 2020

28
2
23
3
2
Q4 2020

26
1
23
2
Q1 2021

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

Countries Procuring TLD

<table>
<thead>
<tr>
<th>Country</th>
<th>Country</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia</td>
<td>Haiti</td>
<td>Papua New Guinea</td>
</tr>
<tr>
<td>Benin</td>
<td>Kenya</td>
<td>Peru</td>
</tr>
<tr>
<td>Botswana</td>
<td>Laos</td>
<td>Rwanda</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>Lesotho</td>
<td>Senegal</td>
</tr>
<tr>
<td>Burundi</td>
<td>Liberia</td>
<td>Sierra Leone</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Madagascar</td>
<td>South Africa</td>
</tr>
<tr>
<td>Cape Verde</td>
<td>Malawi</td>
<td>Tanzania</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>Mali</td>
<td>Timor-Leste</td>
</tr>
<tr>
<td>Chad</td>
<td>Mauritania</td>
<td>Togo</td>
</tr>
<tr>
<td>Congo Brazzaville</td>
<td>Mongolia</td>
<td>Uganda</td>
</tr>
<tr>
<td>Congo DRC</td>
<td>Mozambique</td>
<td>Vietnam</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>Namibia</td>
<td>Yemen</td>
</tr>
<tr>
<td>Eswatini</td>
<td>Niger</td>
<td>Zambia</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Nigeria</td>
<td>Zimbabwe</td>
</tr>
<tr>
<td>Ghana</td>
<td>Pakistan</td>
<td></td>
</tr>
<tr>
<td>Guatemala</td>
<td>Panama</td>
<td></td>
</tr>
</tbody>
</table>

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.

TLD Demand as % of Adult First Line

Q4, 2018 - Q1, 2020

- TLD 44%

November 2018
4th Annual Buyers/Sellers Summit

Q4, 2019 - Q1, 2021

- TLD 77%

November 2019
5th Annual Buyers/Sellers Summit

3x Increase in TLD Volume

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)

TLD 30 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- PEPFAR
- Kenya
- Republic of South Africa
- Global Fund

Q4 2019: 20.0
- PEPFAR: 4.6
- Kenya: 1.7
- Republic of South Africa: 13.0

Q1 2020: 19.0
- PEPFAR: 3.5
- Kenya: 1.3
- Republic of South Africa: 9.3

Q2 2020: 19.4
- PEPFAR: 1.8
- Kenya: 10.0
- Republic of South Africa: 5.8

Q3 2020: 27.6
- PEPFAR: 3.0
- Kenya: 1.8
- Republic of South Africa: 13.9
- Global Fund: 9.0

Q4 2020: 16.6
- PEPFAR: 15.2
- Republic of South Africa: 15.6

Q1 2021: 17.1
- PEPFAR: 16.6
- Republic of South Africa: 17.1

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Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

WORK IN PROGRESS

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TLD 180 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- PEPFAR
- Global Fund

WORK IN PROGRESS

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Comparison of TLD Pack Size by Patient Months

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
Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

<table>
<thead>
<tr>
<th>Quarter</th>
<th>PEPFAR</th>
<th>Kenya</th>
<th>Republic of South Africa</th>
<th>Global Fund</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2019</td>
<td>1.9</td>
<td>0.5</td>
<td>0.5</td>
<td>1.1</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>1.2</td>
<td>0.5</td>
<td>0.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Q2 2020</td>
<td>2.9</td>
<td>0.8</td>
<td>0.7</td>
<td>1.1</td>
</tr>
<tr>
<td>Q3 2020</td>
<td>1.8</td>
<td>0.6</td>
<td>1.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Q4 2020</td>
<td>2.1</td>
<td>1.5</td>
<td>0.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Q1 2021</td>
<td>1.8</td>
<td>0.5</td>
<td>0.5</td>
<td>1.6</td>
</tr>
</tbody>
</table>

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Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- Global Fund

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**SOURCE:** PEPFAR, Government of Kenya, The Global Fund, South Africa
Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- PEPFAR
- Kenya
- Global Fund

**Overall ARV Demand Outlook**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>PEPFAR</th>
<th>Kenya</th>
<th>Global Fund</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2019</td>
<td>0.01</td>
<td>1.83</td>
<td>4.02</td>
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<tr>
<td>Q1 2020</td>
<td></td>
<td></td>
<td>2.17</td>
</tr>
<tr>
<td></td>
<td>0.02</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Q2 2020</td>
<td>0.52</td>
<td></td>
<td>3.21</td>
</tr>
<tr>
<td></td>
<td>0.02</td>
<td></td>
<td>0.13</td>
</tr>
<tr>
<td>Q3 2020</td>
<td>3.07</td>
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<td></td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td>Q4 2020</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 2021</td>
<td>0.53</td>
<td></td>
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</tr>
</tbody>
</table>

**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
TLE 400 90 Tabs – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

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Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- Republic of South Africa
- Global Fund

12.0
13.0
8.2
4.7
3.2
3.1

Q4 2019
Q1 2020
Q2 2020
Q3 2020
Q4 2020
Q1 2021

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

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

<table>
<thead>
<tr>
<th>Year</th>
<th>PEPFAR</th>
<th>Kenya</th>
<th>Republic of South Africa</th>
<th>Global Fund</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2019</td>
<td>2.9</td>
<td>0.3</td>
<td>0.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>1.6</td>
<td>0.2</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Q2 2020</td>
<td>2.4</td>
<td>0.6</td>
<td>0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>Q3 2020</td>
<td>1.6</td>
<td>0.5</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Q4 2020</td>
<td>1.1</td>
<td>1.0</td>
<td>1.0</td>
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<tr>
<td>Q1 2021</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>


WORK IN PROGRESS

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.
EFV 600 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- Republic of South Africa
- Global Fund

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

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- PEPFAR
- Kenya
- Republic of South Africa
- Global Fund

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

#### Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

<table>
<thead>
<tr>
<th>Quarter</th>
<th>PEPFAR</th>
<th>Kenya</th>
<th>Global Fund</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2019</td>
<td>1.0</td>
<td>0.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>0.5</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Q2 2020</td>
<td>0.8</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Q3 2020</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Q4 2020</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Q1 2021</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**WORK IN PROGRESS**

**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
ATV/r 300/100 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

PEPFAR
Kenya
Global Fund

Q4 2019
Q1 2020
Q2 2020
Q3 2020
Q4 2020
Q1 2021

0.6
0.4
0.4
0.5
0.5
0.5

0.4
0.3
0.2
0.2
0.2
0.1

0.5
0.2
0.1

0.1


WORK IN PROGRESS

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LPV/r 200/50 – Consolidated Demand Forecast Outlook

**Overall ARV Demand Outlook**
Q4 2019-Q1 2021, Number of packs, millions

- **PEPFAR**
- **Kenya**
- **Republic of South Africa**
- **Global Fund**

Q4 2019: 1.5
  - PEPFAR: 0.2
  - Kenya: 0.4
  - Republic of South Africa: 0.8
  - Global Fund: 0.2

Q1 2020: 1.9
  - PEPFAR: 0.8
  - Kenya: 0.2
  - Republic of South Africa: 0.8
  - Global Fund: 0.2

Q2 2020: 1.6
  - PEPFAR: 0.3
  - Kenya: 0.2
  - Republic of South Africa: 0.8
  - Global Fund: 0.5

Q3 2020: 1.4
  - PEPFAR: 0.3
  - Kenya: 0.2
  - Republic of South Africa: 0.8
  - Global Fund: 0.8

Q4 2020: 1.1
  - PEPFAR: 0.2
  - Kenya: 0.2
  - Republic of South Africa: 0.8
  - Global Fund: 0.2

Q1 2021: 0.8
  - PEPFAR: 0.2
  - Kenya: 0.2
  - Republic of South Africa: 0.8
  - Global Fund: 0.2

**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
LPV/r 100/25 – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

<table>
<thead>
<tr>
<th>Quarter</th>
<th>PEPFAR</th>
<th>Kenya</th>
<th>Republic of South Africa</th>
<th>Global Fund</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2019</td>
<td>1.6</td>
<td>0.2</td>
<td>0.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>1.5</td>
<td>0.2</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Q2 2020</td>
<td>1.4</td>
<td>0.2</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Q3 2020</td>
<td>1.3</td>
<td>0.2</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Q4 2020</td>
<td></td>
<td></td>
<td>0.15</td>
<td>0.06</td>
</tr>
<tr>
<td>Q1 2021</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

- **PEPFAR**
- Kenya
- Republic of South Africa
- Global Fund

**Overall ARV Demand Forecast Outlook**

**Q4 2019-Q1 2021, Number of packs, millions**

- **Q4 2019**
  - PEPFAR: 0.4
  - Kenya: 0.3
  - Republic of South Africa: 0.1
- **Q1 2020**
  - PEPFAR: 0.4
  - Kenya: 0.3
- **Q2 2020**
  - PEPFAR: 0.7
  - Kenya: 0.3
- **Q3 2020**
  - PEPFAR: 0.7
  - Kenya: 0.3
- **Q4 2020**
  - PEPFAR: 0.1
  - Kenya: 0.4
- **Q1 2021**
  - PEPFAR: 0.02
  - Kenya: 0.1

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

**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.
NVP 100ml Oral Suspension – Consolidated Demand Forecast Outlook

Overall ARV Demand Outlook
Q4 2019-Q1 2021, Number of packs, millions

<table>
<thead>
<tr>
<th>Quarter</th>
<th>PEPFAR</th>
<th>Kenya</th>
<th>Republic of South Africa</th>
<th>Global Fund</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2019</td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>0.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Q2 2020</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Q3 2020</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Q4 2020</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Q1 2021</td>
<td>0.05</td>
<td></td>
<td></td>
<td></td>
<td>0.05</td>
</tr>
</tbody>
</table>

**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
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

First Line ARV Fixed Dose Combinations, GHSC-PSM
Millions of Packs Ordered as of Oct 2019*

- 2006: Patients transitioned off d4T 40
- 2010: TLE and LZN recommended first line
- 2013: EFV with TL or TE recommended preferred first line for patients starting ART
- 2016: DTG with TL or TE recommended as alt first line
- 2017: FDA tentatively approves TLD* (Aug)
- 2019: WHO recommends TLD as first line preferred for all adult and adolescents.

*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

*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

- 25 (89.3%) PEPFAR countries with Routine 3 month MMD
- 3 (10.7%) PEPFAR countries without routine 3 month MMD
PEPFAR Countries with 6 Month MMD policies

6 Month MMD routinely provided

- 14 (50.0%) PEPFAR countries that routinely permit 6 month MMD
- 9 (32.1%) PEPFAR countries where the policy does not permit 6 month MMD
- 5 (17.9%) PEPFAR countries that permit 6 month MMD by exception or clinician judgment only
<table>
<thead>
<tr>
<th>OUs</th>
<th>3 month MMD</th>
<th>6 month MMD</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botswana, the DR, and South Africa</td>
<td>No</td>
<td>No</td>
<td>These three countries do not presently support MMD. All three have draft policies.</td>
</tr>
<tr>
<td>Angola, Burundi, Liberia, Mozambique, Rwanda, South Sudan, eSwatini, Tanzania, Uganda, and Ukraine</td>
<td>✔</td>
<td>No</td>
<td>Policies in these countries do not permit MMD greater than 3 months. Many of them they do permit MMS.</td>
</tr>
<tr>
<td>Cambodia, Kenya, Malawi, Nigeria, and Vietnam</td>
<td>✔</td>
<td>Sometimes</td>
<td>6 month MMD is largely at the discretion of the clinician involved.</td>
</tr>
<tr>
<td>Burma, Cameroon, Côte d’Ivoire, DRC, Ethiopia, Haiti, Lesotho, Namibia, Zambia, Zimbabwe</td>
<td>✔</td>
<td>✔</td>
<td>These countries offer 3-6 month MMD and sometimes more than 6 month MMD.</td>
</tr>
</tbody>
</table>
MMD Policy vs. Supply Chain
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
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

<table>
<thead>
<tr>
<th>Maximum SL</th>
<th>75% RSL</th>
<th>80% RSL</th>
<th>85% RSL</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 months</td>
<td>18 months</td>
<td>19.2 months</td>
<td>20.4 months</td>
</tr>
<tr>
<td>36 months</td>
<td>27 months</td>
<td>28.8 months</td>
<td>30.6 months</td>
</tr>
<tr>
<td>48 months</td>
<td>36 months</td>
<td>38.4 months</td>
<td>40.8 months</td>
</tr>
<tr>
<td>60 months</td>
<td>45 months</td>
<td>48 months</td>
<td>51 months</td>
</tr>
</tbody>
</table>
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.1 available at:
The policy allows for flexibility dependent upon consumption rates

<table>
<thead>
<tr>
<th>Expiry date</th>
<th>RSL at time of dispatch from Manufacturer’s premises</th>
<th>RSL at time of delivery at port of entry of country</th>
<th>RSL at time of delivery at point, after customs clearance</th>
<th>RSL at time of delivery at end-user level</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 months &lt; RSL &lt; 60 months</td>
<td>40 months</td>
<td>30 months</td>
<td>18 months</td>
<td>12 months</td>
</tr>
<tr>
<td>36 months &lt; RSL &lt; 48 months</td>
<td>30 months</td>
<td>24 months</td>
<td>18 months</td>
<td>12 months</td>
</tr>
<tr>
<td>24 months &lt; RSL &lt; 36 months</td>
<td>20 months</td>
<td>15 months</td>
<td>10 months</td>
<td>6 months</td>
</tr>
<tr>
<td>12 to 24 months</td>
<td>9 months</td>
<td>7 months</td>
<td>5 months</td>
<td>3 months</td>
</tr>
<tr>
<td>Less than 12 months</td>
<td>Special arrangements and conditions apply</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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

**Phase 1**
- Tertiary Packaging
  - Homogenous Trade Item
    - GS1 Data Matrix or GS1-128 barcode encoded with:
      - (01) GTIN
      - (10) Batch/lot
      - (17) Expiration Date
- Master Data
  - All item master data submitted through the GDSN®
  - (416) GLN Sold-From
  - (415) GLN Invoice-From
  - (414) GLN Production

**Phase 2**
- Secondary Packaging
  - GTIN for each unit of measure
- Master Data
  - (416) GLN Sold-From
  - (415) GLN Invoice-From
  - (414) GLN Production

**Phase 3**
- Trade Item
  - GS1 Data Matrix encoded with:
    - (01) GTIN
    - (10) Batch/lot
    - (17) Expiration Date

**Phase 4**
- Homogenous Trade Item
  - GS1 Data Matrix or GS1-128 barcode also encoded with:
    - (21) Serial Number
- Mixed or Partial Trade Item
  - GS1-128 barcode encoded with:
    - (00) SSCC
- Logistic Unit
  - GS1-128 barcode encoded with:
    - (00) SSCC
- Trade Item
  - GS1 Data Matrix also encoded with:
    - (21) Serial Number

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

GTIN: Global Trade Item Number
GLN: Global Location Number
GDSN: Global Data Synchronization Network
SSCC: Serial Shipping Container Code
Compliance to date: Identification & Labelling

ARV Compliance as of November 2019

Phase 1 Score (Identification & Labelling - Primary Pack)
Phase 3 Score (Labelling - Secondary Pack)
Phase 4 Score (Labelling - Serialization)
Suppliers synchronizing through GDSN
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

2. Register for Data-pool
   - Data-pools are the mechanism for sending GTIN master data to GHSC-PSM

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 2018

RECOMMENDED
March-June 2019

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
Republic of South Africa

Ms Khadija Jamaloodien
Affordable Medicines Directorate

ARV Large Buyer Seller Summit
November 2019
Day 3
1. Context
2. National Surveillance Centre
3. Barcoding
4. IMAT process
5. Looking forward
ARV stockouts make headlines in SA

Global ingredient shortage behind ARV stockouts in SA

High prevalence of stockouts of antiretroviral medicines in South Africa

Access to medicines & treatment

4th June 2019 | Anjo Thurn
Over recent years the NDoH has made strides in supply chain planning

- Stock visibility system
- National Surveillance Centre
- Provincial Surveillance Centre
- Demand & supply planning
- TLD transition detailed planning
- Alternative distribution channels (CCMDD, GP Care Cell, Automated dispensing solutions)

GP Care Cell Programme
1. Context

2. National Surveillance Centre

3. Barcoding

4. IMAT process

5. Looking forward
SA has automated visibility of a number of KPIs

<table>
<thead>
<tr>
<th>KPI</th>
<th>TARGET (%)</th>
<th>KEY:</th>
<th>AS VS SCORE (Hover to see more detail)</th>
<th>TREND (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEPOT AVAILABILITY</td>
<td>90%</td>
<td><strong>GREEN</strong>: Medicine Availability % &gt; 90%</td>
<td>77.01%</td>
<td>77.07%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>AMBER</strong>: Medicine Availability % &lt; 90% but &gt; 80%</td>
<td>65.20%</td>
<td>74.70%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>RED</strong>: Medicine Availability % &lt; 80%</td>
<td>57.07%</td>
<td>73.72%</td>
</tr>
<tr>
<td>ECD MD AVAILABILITY</td>
<td>90%</td>
<td><strong>GREEN</strong>: Medicine Availability % &gt; 90%</td>
<td>82.28%</td>
<td>82.40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>AMBER</strong>: Medicine Availability % &lt; 90% but &gt; 80%</td>
<td>87.70%</td>
<td>82.27%</td>
</tr>
<tr>
<td>HOSPITAL AVAILABILITY</td>
<td>90%</td>
<td><strong>GREEN</strong>: Medicine Availability % &gt; 90%</td>
<td>87.70%</td>
<td>87.72%</td>
</tr>
<tr>
<td>CLINIC AVAILABILITY</td>
<td>90%</td>
<td><strong>GREEN</strong>: Medicine Availability % &gt; 90%</td>
<td>87.70%</td>
<td>87.72%</td>
</tr>
<tr>
<td>IN FULL:</td>
<td>90%</td>
<td><strong>GREEN</strong>: % of Deliveries delivered in full &gt; 90%</td>
<td>57.52%</td>
<td>57.52%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>AMBER</strong>: % of Deliveries delivered in full &lt; 90%</td>
<td>57.52%</td>
<td>57.52%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>RED</strong>: % of Deliveries delivered in full &lt; 80%</td>
<td>57.52%</td>
<td>57.52%</td>
</tr>
<tr>
<td>ON TIME:</td>
<td>90%</td>
<td><strong>GREEN</strong>: % of Deliveries delivered on time &gt; 90%</td>
<td>67.87%</td>
<td>66.84%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>AMBER</strong>: % of Deliveries delivered on time &lt; 90%</td>
<td>67.87%</td>
<td>57.61%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>RED</strong>: % of Deliveries delivered on time &lt; 80%</td>
<td>67.87%</td>
<td>57.61%</td>
</tr>
<tr>
<td>ON TIME IN FULL (OTIF):</td>
<td>90%</td>
<td><strong>GREEN</strong>: % of Deliveries delivered on time and in full &gt; 90%</td>
<td>55.69%</td>
<td>64.76%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>AMBER</strong>: % of Deliveries delivered on time and in full &lt; 90%</td>
<td>55.69%</td>
<td>55.33%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>RED</strong>: % of Deliveries delivered on time and in full &lt; 80%</td>
<td>55.69%</td>
<td>55.33%</td>
</tr>
<tr>
<td>SUPPLIER CAPACITY:</td>
<td>100%</td>
<td><strong>GREEN</strong>: SUPPLIERS can meet demand for 100% of the ITEMS</td>
<td>70.55%</td>
<td>81.06%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>AMBER</strong>: SUPPLIERS can meet demand for &lt; 100% of the ITEMS</td>
<td>70.55%</td>
<td>81.06%</td>
</tr>
<tr>
<td>PAYMENTS OVERDUE:</td>
<td>90%</td>
<td><strong>GREEN</strong>: % of Current Debt over Total Debt &lt; 90%</td>
<td>66.55%</td>
<td>91.75%</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>AMBER</strong>: % of Current Debt over Total Debt &gt; 90%</td>
<td>66.55%</td>
<td>91.75%</td>
</tr>
</tbody>
</table>
...with information to facility level

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

<table>
<thead>
<tr>
<th>FACILITY TYPE GROUP:</th>
<th>NUMBER OF FACILITIES REPORTING:</th>
<th>2019/20 TARGETS:</th>
<th>2019/20 RESULT:</th>
<th>2020/21 TARGET:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depot:</td>
<td>23 Facilities</td>
<td>Q1: 44</td>
<td>Q2: 44</td>
<td>Q3: 49</td>
</tr>
<tr>
<td>CCMDD:</td>
<td>8 Facilities</td>
<td></td>
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<tr>
<td>Other: GP Carecell/PDU</td>
<td>57 Facilities</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hospital:</td>
<td>373 Facilities</td>
<td>Q1: 340</td>
<td>Q2: 350</td>
<td>Q3: 365</td>
</tr>
<tr>
<td>Clinic:</td>
<td>3,272 Facilities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL:</td>
<td>3,733 Facilities</td>
<td>Q1: 3574</td>
<td>Q2: 3621</td>
<td>Q3: 3682</td>
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</tbody>
</table>

FACILITIES SUMMARY:
>90% National Medicine Availability for All ARVs

Overall Medicine Availability for ARVs:
- 91.6%

Overall Medicine Availability for ARVs per Month:
- Nov-18: 91.0%
- Dec-18: 92.0%
- Jan-19: 91.4%
- Feb-19: 91.6%
- Mar-19: 91.9%
- Apr-19: 91.2%
- May-19: 91.0%
- Jun-19: 91.9%
- Jul-19: 91.5%
- Aug-19: 91.1%
- Sep-19: 91.3%
- Oct-19: 91.9%
...with TEE 300/200/600 at 99%
2 provinces require focus
Medicine Availability for All ARVs

<table>
<thead>
<tr>
<th>Overall Medicine Availability for ARVs per Province</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Cape</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>90.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Medicine Availability for ARVs per Province/Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov-18</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>88.6%</td>
</tr>
<tr>
<td>Dec-18</td>
</tr>
<tr>
<td>Jan-19</td>
</tr>
<tr>
<td>Feb-19</td>
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<tr>
<td>Mar-19</td>
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<tr>
<td>Apr-19</td>
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<tr>
<td>May-19</td>
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<tr>
<td>Jun-19</td>
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<tr>
<td>Jul-19</td>
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<tr>
<td>Aug-19</td>
</tr>
<tr>
<td>Sep-19</td>
</tr>
<tr>
<td>Oct-19</td>
</tr>
</tbody>
</table>
ABC/3TC 600/300 has been a real challenge, but now recovered...
ABC/3TC 600/300 Provincial Medicine Availability

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

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Cape</td>
<td>91.2%</td>
<td>90.0%</td>
<td>87.9%</td>
<td>91.0%</td>
<td>94.0%</td>
<td>93.5%</td>
<td>92.6%</td>
<td>91.8%</td>
<td>89.5%</td>
<td>95.1%</td>
<td>80.8%</td>
<td>85.1%</td>
<td>85.4%</td>
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<tr>
<td>Free State</td>
<td>49.9%</td>
<td>91.1%</td>
<td>85.9%</td>
<td>95.9%</td>
<td>91.3%</td>
<td>88.3%</td>
<td>73.1%</td>
<td>68.3%</td>
<td>82.4%</td>
<td>93.2%</td>
<td>81.8%</td>
<td>90.6%</td>
<td>95.0%</td>
</tr>
<tr>
<td>Gauteng</td>
<td>82.4%</td>
<td>94.0%</td>
<td>92.0%</td>
<td>94.1%</td>
<td>98.4%</td>
<td>93.0%</td>
<td>94.7%</td>
<td>70.0%</td>
<td>82.7%</td>
<td>60.9%</td>
<td>53.8%</td>
<td>57.8%</td>
<td>95.4%</td>
</tr>
<tr>
<td>KwaZulu-Natal</td>
<td>83.5%</td>
<td>88.0%</td>
<td>91.6%</td>
<td>91.6%</td>
<td>90.6%</td>
<td>89.1%</td>
<td>93.9%</td>
<td>70.5%</td>
<td>70.7%</td>
<td>45.5%</td>
<td>44.7%</td>
<td>58.1%</td>
<td>84.1%</td>
</tr>
<tr>
<td>Limpopo</td>
<td>74.6%</td>
<td>77.3%</td>
<td>76.7%</td>
<td>74.9%</td>
<td>70.1%</td>
<td>80.0%</td>
<td>65.4%</td>
<td>60.6%</td>
<td>58.8%</td>
<td>45.7%</td>
<td>44.7%</td>
<td>58.1%</td>
<td>58.1%</td>
</tr>
<tr>
<td>Mpumalanga Province</td>
<td>64.9%</td>
<td>90.5%</td>
<td>90.3%</td>
<td>94.2%</td>
<td>70.6%</td>
<td>69.2%</td>
<td>61.2%</td>
<td>72.0%</td>
<td>65.7%</td>
<td>49.7%</td>
<td>42.0%</td>
<td>82.1%</td>
<td>96.1%</td>
</tr>
<tr>
<td>North West Province</td>
<td>94.8%</td>
<td>93.3%</td>
<td>93.3%</td>
<td>93.3%</td>
<td>100.0%</td>
<td>62.5%</td>
<td>79.6%</td>
<td>93.0%</td>
<td>55.7%</td>
<td>56.9%</td>
<td>39.3%</td>
<td>39.3%</td>
<td>98.2%</td>
</tr>
<tr>
<td>Northern Cape</td>
<td>99.9%</td>
<td>94.8%</td>
<td>93.3%</td>
<td>93.3%</td>
<td>93.3%</td>
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<td>92.5%</td>
<td>92.5%</td>
</tr>
</tbody>
</table>
Stockouts in AZT/3TC 300/150 but also stabilised now

<table>
<thead>
<tr>
<th>Overall Medicine Availability % per Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>84.4%</td>
</tr>
</tbody>
</table>
Of concern is a slightly declining trend in supplier performance.
Contents

1. Context

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5. Looking forward
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
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
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1. Context

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“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
# 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
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## Selected items from Hot List

<table>
<thead>
<tr>
<th>PRODUCT DETAILS</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACTIVE PHARMACEUTICAL INGREDIENT</strong></td>
<td><strong>ROOT CAUSE</strong></td>
</tr>
<tr>
<td><strong>ABACAVIR and LAMIVUDINE tablet</strong></td>
<td>API Issue (Shortage); High Uptake</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>High Uptake</td>
</tr>
<tr>
<td><strong>Lamivudine</strong></td>
<td>API Issue (Shortage)</td>
</tr>
<tr>
<td><strong>Levonorgestrel, Ethinyl Estradiol, Triphasic</strong></td>
<td>High Uptake; Manufacturing Constraint</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td><strong>Nevirapine</strong></td>
<td>High Uptake</td>
</tr>
<tr>
<td><strong>Norethisterone enanthate</strong></td>
<td>High Uptake (Due to Shortages of Alternate Commodities)</td>
</tr>
<tr>
<td><strong>Norgestrel, Ethinyl Estradiol</strong></td>
<td>High Uptake; Manufacturing Constraint</td>
</tr>
<tr>
<td><strong>Subdermal Implant Containing Etonogestrel</strong></td>
<td>Manufacturing Constraints (Global Capacity Issue)</td>
</tr>
<tr>
<td><strong>Zidovudine</strong></td>
<td>Manufacturing Constraints (Production Capacity)</td>
</tr>
</tbody>
</table>
Contents

1. Context
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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 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
Kenya: Supply Chain Optimization-Data Visibility and Use for Decision-Making
Architecture: Commodity data Reporting, management and Pipeline Monitoring

Transactional data at service delivery Points (Manual & Electronic Tools)

Summaries/Aggregation

FCDRR; FMAPS
SOH, Issues, Receipts, Patients/Regimen data

Reporting (MOH 729, 731)

On line DHIS 2
Aggregation, Analysis

KEMSA ERP (SOH, Receipts, Orders, Planned Call-downs, Issues)

Data Sharing

NASCOP ART COMMODITY
MANAGER (Dashboards; Trackers, Order Management Decisions)

Data Sharing

DHIS2: District Health Information System- Open Source Health Management Data Platform
**DHIS2- Facility MoH 731 Form (FCDRR)**

**Nakuru Provincial General Hospital - September 2019**

Completed by: Lmomanyi

**Data Set Report**
- [Data criteria](#)
- [Download as Excel](#)
- [Download as PDF](#)
- [Print](#)

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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Unit pack size</th>
<th>Beginning Balance</th>
<th>Total Quantity Received this month</th>
<th>Total Quantity Dispensed this month</th>
<th>Losses &amp; Wastage</th>
<th>Pos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir (ABC) 300mg Tablets</td>
<td>60s</td>
<td>3</td>
<td>23</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir/Lamivudine (ABC/3TC) 600mg/300mg FDC Tablets</td>
<td>60s</td>
<td>53</td>
<td>800</td>
<td>497</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir/Ritonavir (ATV/r) 300/100mg Tablets</td>
<td>30s</td>
<td>1479</td>
<td>500</td>
<td>472</td>
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<td></td>
</tr>
<tr>
<td>Darunavir (DRV) 600mg Tablets</td>
<td>60s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dolutegravir(DTG) 50mg tabs</td>
<td>30s</td>
<td>78</td>
<td>39</td>
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<td></td>
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<tr>
<td>Efavirenz (EFV) 400mg Tablets</td>
<td>30s</td>
<td>70</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Efavirenz (EFV) 600mg Tablets</td>
<td>30s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### DHIS2: MOH 731/ FCDRR Aggregated Data (Kenya)

#### Kenya - September 2019

Write a comment, question or interpretation of this report

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Unit pack size</th>
<th>Beginning Balance</th>
<th>Total Quantity Received this month</th>
<th>Total Quantity Dispensed this month</th>
<th>Losses &amp; Wastage</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir (ABC) 300mg Tablets</td>
<td>60s</td>
<td>11304</td>
<td>767</td>
<td>1520</td>
<td>8</td>
<td>245</td>
</tr>
<tr>
<td>Abacavir/Lamivudine (ABC/3TC) 600mg/300mg FDC Tablets</td>
<td>60s</td>
<td>53716</td>
<td>36106</td>
<td>32236</td>
<td>6</td>
<td>2957</td>
</tr>
<tr>
<td>Atazanavir/Ritonavir (ATV/r) 300/100mg Tablets</td>
<td>30s</td>
<td>120323</td>
<td>99512</td>
<td>89633</td>
<td>485</td>
<td>1879</td>
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<tr>
<td>Darunavir (DRV) 600mg Tablets</td>
<td>60s</td>
<td>296</td>
<td>152</td>
<td>185</td>
<td>16</td>
<td>30</td>
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<td>Dolutegravir(DTG) 50mg tabs</td>
<td>30s</td>
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<td>9672</td>
<td>8041</td>
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<tr>
<td>Efavirenz (EFV) 400mg Tablets</td>
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<td>247</td>
<td>2</td>
<td>7</td>
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<td>Efavirenz (EFV) 600mg Tablets</td>
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<td>36904</td>
<td>2332</td>
<td>4422</td>
<td>462</td>
<td>422</td>
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<tr>
<td>Etravirine (ETV) 200mg Tablets</td>
<td>60s</td>
<td>648</td>
<td>308</td>
<td>326</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>
DHIS2: MOH 729/F-MAPS Aggregated Data

**Data Set Report**

Kenya - September 2019

Write a comment, question or interpretation of this report

<table>
<thead>
<tr>
<th>Regimen Code</th>
<th>ARV or OI Treatment Regimen</th>
<th>Number of Current Active Patients/Clients on this regimen at the end of this Reporting period</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF1A</td>
<td>AZT + 3TC + NVP</td>
<td>10519</td>
</tr>
<tr>
<td>AF1B</td>
<td>AZT + 3TC + EFV</td>
<td>4154</td>
</tr>
<tr>
<td>AF1D</td>
<td>AZT + 3TC + DTG</td>
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<td>AF2A</td>
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<td>4910</td>
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<tr>
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<td>TDF + 3TC + EFV</td>
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<tr>
<td>AF2D</td>
<td>TDF + 3TC + ATV/r</td>
<td>9122</td>
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<tr>
<td>AF2E</td>
<td>TDF + 3TC + DTG</td>
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<tr>
<td>AF2F</td>
<td>TDF + 3TC + LPV/r (1L Adults &lt;40kg)</td>
<td>1549</td>
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### DHIS2: Pivot Tables (Adult ART Optimization)

#### TLD AND TLE

<table>
<thead>
<tr>
<th>Period / Data</th>
<th>Kenya</th>
<th>Kenya</th>
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<td>November 2018</td>
<td>66,626</td>
<td>503,864</td>
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<td>December 2018</td>
<td>94,266</td>
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<td>February 2019</td>
<td>232,743</td>
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<td>March 2019</td>
<td>312,614</td>
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<td>May 2019</td>
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<tr>
<td>June 2019</td>
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<td>July 2019</td>
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<td>August 2019</td>
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<td>September 2019</td>
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<td>October 2019</td>
<td>451,322</td>
<td>437,783</td>
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**Data Source:** MoH 7298 Facility - F'MAPS Revision 2017 TDF + 3TC + DTG AF2E Adult ART 1st Line regimens
ART Optimization

Phase-out of NVP Paed Regimens

Adult 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

Dashboard

Reporting Rates Trend
Source: www.commodities.nascop.org

Regimen Patient Numbers
Source: www.commodities.nascop.org
Commodity Manager: Patients by Regimen

### Regimen Patient Numbers

**Source:** www.commodities.nascop.org

<table>
<thead>
<tr>
<th>Regimen Line</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adult First Line</strong></td>
<td>924,361</td>
</tr>
<tr>
<td><strong>Adult Second Line</strong></td>
<td>83,832</td>
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<tr>
<td><strong>Paediatric First Line</strong></td>
<td>55,681</td>
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<tr>
<td><strong>Paediatric Second Line</strong></td>
<td>8,548</td>
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<tr>
<td><strong>Adult Third Line</strong></td>
<td>870</td>
</tr>
<tr>
<td><strong>Paediatric Third Line</strong></td>
<td>40</td>
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### Regimen Patient Numbers

**Source:** www.commodities.nascop.org

<table>
<thead>
<tr>
<th>Regimen</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF2E</td>
<td>TDF + 3TC + DTG</td>
</tr>
<tr>
<td>AF2B</td>
<td>TDF + 3TC + EFV</td>
</tr>
<tr>
<td>AF1A</td>
<td>AZT + 3TC + NVP</td>
</tr>
<tr>
<td>AF2D</td>
<td>TDF + 3TC + ATV/r</td>
</tr>
<tr>
<td>AF2A</td>
<td>TDF + 3TC + NVP</td>
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<tr>
<td>AF1B</td>
<td>AZT + 3TC + EFV</td>
</tr>
<tr>
<td>AF4B</td>
<td>ABC + 3TC + EFV</td>
</tr>
<tr>
<td>AF4C</td>
<td>ABC + 3TC + DTG</td>
</tr>
<tr>
<td>AF5X</td>
<td>All other 1st line Adult re...</td>
</tr>
<tr>
<td>AF1D</td>
<td>AZT + 3TC + DTG</td>
</tr>
<tr>
<td>AF2F</td>
<td>TDF + 3TC + LPV/r (1L A...</td>
</tr>
<tr>
<td>AF4A</td>
<td>ABC + 3TC + NVP</td>
</tr>
<tr>
<td>AF2H</td>
<td>TDF + FTC + ATV/r</td>
</tr>
</tbody>
</table>
Commodity Manager: Pediatric Patients by Regimen

Regimen Patient Numbers

Source: www.commodities.nascop.org

- CF2B | ABC + 3TC + EFV: 28,881 patients
- CF2D | ABC + 3TC + LPV/r: 12,487 patients
- CF4B | TDF + 3TC + EFV: 3,341 patients
- CF1A | AZT + 3TC + NVP: 2,572 patients
- CF2A | ABC + 3TC + NVP: 2,258 patients
- CF1C | AZT + 3TC + LPV/r: 2,123 patients
- CF1B | AZT + 3TC + EFV: 1,900 patients
- All other 1st line Paediatric regimens: 1,005 patients
- CF4D | TDF + 3TC + ATV/r: 418 patients
- CF2E | ABC + 3TC + ATV/r: 389 patients
- CF4C | TDF + 3TC + LPV/r: 262 patients
- CF1D | AZT + 3TC + ATV/r: 199 patients
- CF4A | TDF + 3TC + NVP: 141 patients
- CF1E | AZT + 3TC + RAL: 41 patients
- CF2F | ABC + 3TC + RAL: 22 patients

Regimen Patient Numbers

Source: www.commodities.nascop.org

- CS2A | ABC + 3TC + LPV/r: 3,582 patients
- CS1A | AZT + 3TC + LPV/r: 740 patients
- CS1B | AZT + 3TC + ATV/r: 512 patients
- CS4X | All other 2nd line Paediatric regimens: 333 patients
- CS2C | ABC + 3TC + ATV/r: 330 patients

No. of Patients

- Art paediatric_first_line
- Art paediatric_second_line
# Pipeline Monitoring Using the Commodity Tracker
## ABC/3TC 120/60MG

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

#### Transactions

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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<th></th>
<th></th>
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<tr>
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<td>268,864</td>
<td>282,645</td>
<td>232,814</td>
<td>185,453</td>
<td>191,752</td>
<td>357,284</td>
<td>593,051</td>
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<td>Proposed Qty.</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Contracted Qty.</td>
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<td>-</td>
<td>998,158</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
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<tr>
<td>Call Down Qty.</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Received Qty.</td>
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<td>84,683</td>
<td>262,652</td>
<td>309,736</td>
<td>181,436</td>
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<tr>
<td>Issues to Facility</td>
<td>100,122</td>
<td>93,221</td>
<td>83,585</td>
<td>49,829</td>
<td>101,535</td>
<td>78,378</td>
<td>97,087</td>
<td>73,966</td>
<td>97,110</td>
<td>64,238</td>
<td>8,975</td>
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<tr>
<td>Adjustments/Losses (+/-)</td>
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<td>-</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>-19</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Closing Balance</td>
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<td>-</td>
<td>268,864</td>
<td>282,645</td>
<td>232,814</td>
<td>185,457</td>
<td>191,764</td>
<td>357,298</td>
<td>593,057</td>
<td>613,135</td>
<td>920,732</td>
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<td>Monthly Consumption</td>
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<td>76,263</td>
<td>74,132</td>
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<td>77,530</td>
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<td>89,541</td>
<td>78,770</td>
<td>78,573</td>
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<tr>
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<td>100,185</td>
<td>101,176</td>
<td>89,674</td>
<td>94,610</td>
<td>84,445</td>
<td>83,939</td>
<td>80,730</td>
<td>82,984</td>
<td>85,386</td>
<td>69,959</td>
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<tr>
<td>Average Consumption</td>
<td>77,148</td>
<td>76,731</td>
<td>77,436</td>
<td>78,869</td>
<td>77,744</td>
<td>79,590</td>
<td>79,026</td>
<td>81,239</td>
<td>82,012</td>
<td>81,005</td>
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## Procurement Tracker

### Procurement Form

<table>
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<th>Months of Stock (MOS)</th>
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<td>539,509</td>
<td>5.3</td>
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| System Calculated Order Quantity | 992,456 |

### Procurement Quantities

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<th>year</th>
<th>month</th>
<th>proposed</th>
<th>contracted</th>
<th>caldown</th>
<th>received</th>
<th>comments</th>
<th>funding_agents</th>
<th>suppliers</th>
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<td>Jan</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<td></td>
</tr>
<tr>
<td>8</td>
<td>2019</td>
<td>Feb</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>8</td>
<td>2019</td>
<td>Mar</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>8</td>
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<td>108</td>
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<td>0</td>
<td>227420</td>
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</table>
# Commodity Manager: Decisions Tracker

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

<table>
<thead>
<tr>
<th>Discussions</th>
<th>Recommendations</th>
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<tr>
<td><strong>14 Nov/19</strong></td>
<td>- KEMSA to follow up with expected supplies for clearance and distribution.</td>
</tr>
</tbody>
</table>

At 4 MOS. Pending USAID: 229,144 delivery expected by mid-Oct 2019  Pending GF:- 148,650 already in sea

| **11 Oct/19** | - KEMSA to follow up with expected supplies for clearance and distribution. |

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

| **13 Sep/19** | - KEMSA to follow up with expected supplies for clearance and distribution. |

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

| **16 Aug/19** | - KEMSA to follow up with expected supplies for clearance and distribution. |

At 3 MOS. 115,856 re 6th August USAID: 200,000: 170,859 in country- under clearance, 29,144 awaiting shipping documents. Balance is 200,000. GF: 796,319 packs: 115,849 received, 129,382 expected by 26th August 2019, pending balances of 200,000.
## Commodity Manager: Order Management (1)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Expiry Date</th>
<th>End Month Stock on Hand</th>
<th>Days Out of Stock</th>
<th>Resupply Quantity</th>
<th>AMC</th>
<th>Facility MOS</th>
<th>AutoCalc Resupply</th>
<th>Allocated</th>
<th>Allocated MOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir/Emtricitabine 300/200mg FDC</td>
<td>26</td>
<td>0</td>
<td>3</td>
<td>8.67</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir/Lamivudine 300/300mg FDC</td>
<td>160</td>
<td>30</td>
<td>39</td>
<td>4.10</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>Tenofovir/Lamivudine (TDF/3TC/EFV) 300/3 FDC Tabs</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir/Lamivudine (TDF/3TC/EFV) 300/3 FDC Tabs</td>
<td>1434</td>
<td>694</td>
<td>2.07</td>
<td>648</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Adult First Line

- **Code | Regimen**: 
  - AF1A | AZT + 3TC + NVP
  - AF1B | AZT + 3TC + EFV
  - AF2B | TDF + 3TC + EFV
  - AF4B | ABC + 3TC + EFV
  - AF1D | AZT + 3TC + DTG
  - AF2E | TDF + 3TC + DTG

- **No. of Patients**: 
  - 10
  - 12
  - 562
  - 1
  - 4
  - 380
### Commodity Manager: Order Management (2)

<table>
<thead>
<tr>
<th>Code</th>
<th>Regimen</th>
<th>No. of Patients</th>
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<tbody>
<tr>
<td>AF1A</td>
<td>AZT + 3TC + NVP</td>
<td>10</td>
</tr>
<tr>
<td>AF1B</td>
<td>AZT + 3TC + EFV</td>
<td>12</td>
</tr>
<tr>
<td>AF2B</td>
<td>TDF + 3TC + EFV</td>
<td>562</td>
</tr>
<tr>
<td>AF4B</td>
<td>ABC + 3TC + EFV</td>
<td>1</td>
</tr>
<tr>
<td>AF1D</td>
<td>AZT + 3TC + DTG</td>
<td>4</td>
</tr>
<tr>
<td>AF2E</td>
<td>TDF + 3TC + DTG</td>
<td>380</td>
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<table>
<thead>
<tr>
<th>Drug Name</th>
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<th>AutoCalc Resupply</th>
<th>Allocated</th>
<th>Allocated MOS</th>
<th>Comments</th>
<th>Decision</th>
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</thead>
<tbody>
<tr>
<td>Tenofovir/Emtricitabine 300/200mg FDC</td>
<td>26</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir/Lamivudine 300/300mg FDC</td>
<td>160</td>
<td>39</td>
<td>0</td>
<td>30</td>
<td>1</td>
<td>MONITOR</td>
</tr>
<tr>
<td>Tenofovir/Lamivudine. (TDF/3TC/EFV) 300/3 FDC Tabs</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td>RE SUPPLY</td>
</tr>
<tr>
<td>Tenofovir/Lamivudine. (TDF/3TC/EFV) 300/3 FDC Tabs</td>
<td>1434</td>
<td>694</td>
<td>648</td>
<td></td>
<td></td>
<td>RE SUPPLY</td>
</tr>
</tbody>
</table>
Commodity Manager: Communication


- 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

### Table: Number of Patients on ART

<table>
<thead>
<tr>
<th>Key Regimen</th>
<th>No. of Patients on ART</th>
<th>% Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>3,281,912</td>
<td>100%</td>
</tr>
<tr>
<td>Pediatric</td>
<td>1,861,492</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table: Scale-up Numbers

<table>
<thead>
<tr>
<th>Key Regimen</th>
<th>No. of Patients on ART</th>
<th>% Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>3,281,912</td>
<td>100%</td>
</tr>
<tr>
<td>Pediatric</td>
<td>1,861,492</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table: Patients by Regimen (# & %)

<table>
<thead>
<tr>
<th>Key Regimen</th>
<th>No. of Patients on ART</th>
<th>% Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>3,281,912</td>
<td>100%</td>
</tr>
<tr>
<td>Pediatric</td>
<td>1,861,492</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table: SOH at Facility level (MOS)

<table>
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<th>Facility</th>
<th>No. of Patients on ART</th>
<th>% Population</th>
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<td>Facility</td>
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<td>100%</td>
</tr>
<tr>
<td>Facility</td>
<td>1,861,492</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table: SOH at KEMSA (MOS)

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<th>No. of Patients on ART</th>
<th>% Population</th>
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<td>KEMSA</td>
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<td>100%</td>
</tr>
<tr>
<td>KEMSA</td>
<td>1,861,492</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table: Quantities on order (MOS)

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<th>No. of Patients on ART</th>
<th>% Population</th>
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</thead>
<tbody>
<tr>
<td>Quantity</td>
<td>3,281,912</td>
<td>100%</td>
</tr>
<tr>
<td>Quantity</td>
<td>1,861,492</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table: Red-flag items

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
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<tr>
<td>Item</td>
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<td>Item</td>
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</table>
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 1\textsuperscript{st} 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)
1\textsuperscript{st} Line Adult Regimens – CTC2 data
## Adults first line ARV regimens (existing clients)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
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<td>39.5%</td>
<td>54.0%</td>
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<td>TDF /3TC/EFV</td>
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<tr>
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<td>0.0%</td>
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<tr>
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<td>0.1%</td>
<td>2%</td>
<td>5.0%</td>
<td>5.0%</td>
</tr>
</tbody>
</table>
1<sup>st</sup> Line Pediatric Regimens – CTC2 data

![Bar chart showing distribution of 1<sup>st</sup> line pediatric regimens over different periods from Jan-March 2019 to July-Sep 2019.](chart_image)
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!
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
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.
Supply Chain Stakeholder, Insights, Tools, and Data Providers

Manufacturer

GSC

CMS

Pharmacy

Provider

Patient

API

Supply

Procurement

Shipment

Inventory

Issuance

Dispensing

Demand

Prescription

Health

Status

Consumption

Quantification

Forecasting

Supply Plans

Orders

Warehouse

ADVISER

SC-FACT

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

<table>
<thead>
<tr>
<th>AFRICA</th>
<th>AFRICA (cont.)</th>
<th>AFRICA (cont.)</th>
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</thead>
<tbody>
<tr>
<td>TA</td>
<td>PROC</td>
<td>LMD</td>
</tr>
<tr>
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<tr>
<td>Angola</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Botswana</td>
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<tr>
<td>DRC</td>
<td>■</td>
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<tr>
<td>Eswatini</td>
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<td>■</td>
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<td>Ethiopia</td>
<td>■</td>
<td>■</td>
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<td>Kenya</td>
<td>■</td>
<td></td>
</tr>
<tr>
<td>Lesotho</td>
<td>■</td>
<td></td>
</tr>
<tr>
<td>Malawi</td>
<td>■</td>
<td>■</td>
</tr>
</tbody>
</table>

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 *. 

---

USAID Global Health Supply Chain Program
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

### 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.

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

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

### GHSC-PSM orders
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

**Data Collection, Review and Context**
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

Country Context

ARTMIS → PEPFAR Shipments

← WMS – Inventory Data from Warehouses

Pipeline – Future PEPFAR Orders

Legend: (Hover to see series)
- Orders - USAID
- Orders - GF
- Orders - Other
- Proj Orders - USAID
- Proj Orders - GF
- Proj Orders - Other
- WH/AMC
- WH
- MOS
- MOS - 0
- MOS - 1
- MOS - 2
- MOS - 3
- MOS - 4
- MOS - 5
- MOS - 6
- MOS - 7
- MOS - 8
- MOS - 9

Notes:
- 04 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.

USAID Global Health Supply Chain Program
# Warehouse ADVISER: What You Will See

- **Orders - USAID**
- **Orders - GF**
- **Orders - Other**
- **Proj Orders - USAID**
- **Proj Orders - GF**
- **Proj Orders - Other**
- **AMI/AMC**
- **Actual MOS**
- **Proj AMI/AMC**
- **Proj MOS**
- **MOS = 3**
- **MOS = 6**

- 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

USAID Global Health Supply Chain Program
TLE 600 SoH Reported as of September 2019 by Country
More than 20 HIV/AIDS Commodities monitored at 14,000 Service Delivery Points (SDPs) under SC-FACT in 17 countries since September 2018

ARVs –
Adult, Pediatric

RTKs

IPT
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

INFORMATION 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
<table>
<thead>
<tr>
<th>Country</th>
<th>Status</th>
<th>Data Type</th>
<th>Reporting Frequency</th>
<th>Reporting Lag</th>
<th>Reporting Period</th>
<th>Number of Facilities</th>
<th>Number of Products</th>
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<td>Angola</td>
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<td>Monthly</td>
<td>One Month</td>
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<td>Monthly</td>
<td>One Month</td>
<td>2019-07</td>
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<td>Monthly</td>
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<td>Monthly</td>
<td>One Month</td>
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<tr>
<td>DRC</td>
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<td>eSwatini</td>
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<td>Ethiopia</td>
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<td>Monthly</td>
<td>Two Months</td>
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<tr>
<td>Haiti</td>
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<td>Monthly</td>
<td>One Month</td>
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<td>2019-08</td>
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<td>Once every 2 months</td>
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<td>Rwanda</td>
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<td>One Month</td>
<td>2019-09</td>
<td>1748</td>
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</tbody>
</table>
Country Diagnostics & Mitigation (CDM) Tool

- Developed CDMs for 8 Countries:
  - Botswana
  - Namibia
  - Haiti
  - Nigeria
  - Lesotho
  - Zimbabwe
  - Mozambique
  - Zambia

- Conducting Workshop:
  - Enable PMUs and Field Offices to better use the CDM tool
Data Triangulation

Ideal

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

Vs

Reality

• Issuance with no drug dispensing
Data Quality Index

**System**

- **Accessibility**: extent to which data is available, or easily and quickly retrievable
- **Timeliness**: extent to which the data is up-to-date
- **Completeness**: extent to which data is not missing
- **Interpretability**: extent to which data is in appropriate languages, symbols, units, and definitions are clear

**Quality**

- **Ease of Manipulation**: extent to which data is easy to manipulate
- **Free-of-Error**: extent to which data is correct and reliable
- **Consistent Representation**: extent to which data is presented in the same format
- **Understandability**: extent to which data is easily comprehended
## Draft Ranking of Tier 1, Tier 2 Countries (weighted scores)

<table>
<thead>
<tr>
<th>Country</th>
<th>Zimbabwe</th>
<th>Namibia</th>
<th>Rwanda</th>
<th>Cote d'Ivoire</th>
<th>Lesotho</th>
<th>Haiti</th>
<th>Angola</th>
<th>Mozambique</th>
<th>Nigeria</th>
<th>Zambia</th>
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<td>10</td>
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<td>Completeness</td>
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<td>3.64</td>
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<tr>
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<td>48.79</td>
<td>49.22</td>
<td>51.86</td>
<td>53.10</td>
<td>60.11</td>
<td>61.46</td>
<td>64.32</td>
<td>69.83</td>
<td>75.76</td>
</tr>
</tbody>
</table>
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
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.

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...