Introducing New ARV Products In Swaziland:

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Presentation Outline

Introduction to Swaziland

- HIV burden
- Plan to introduce DTG
- Experience with Treatment Guidelines
  - New Products
    - D4T
    - ATV/r
    - TDF/3TC/EFV
  - New Guidelines
    - Routine Viral Load Monitoring
    - Test and Start
- Next Steps

HIV Background

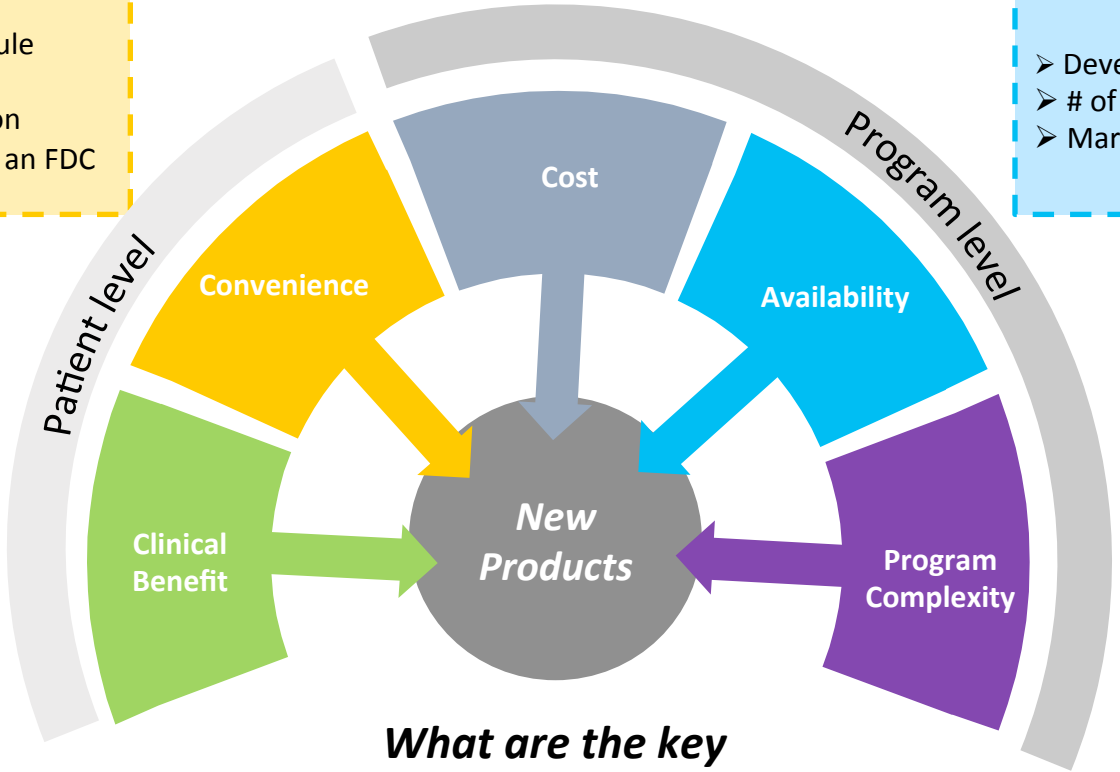
- Population of 1.4 million people
- HIV prevalence 26%
- Incidence : 1.4 (2016)
- ART Coverage = 77 % of all PLHIV
- Good retention and viral suppression rates
- 90-90-90 targets - 85:87:92

OVERVIEW OF NEW PRODUCT EVALUATIONS

- Current pricing
- Future pricing
- Related costs

- Dosing schedule
- Pill burden
- Administration
- Availability as an FDC

- Development pipeline
- # of suppliers
- Marketplace concerns



- Efficacy
- Toxicities
- Side effects
- Contraindications
- Durability
- Drug interactions

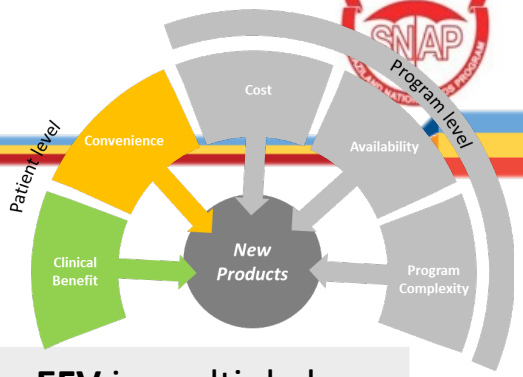
- Special populations
- HCW training & comfort
- Country capacity

What are the key considerations?

Introduction of TDF/ 3TC/DTG (TLD) : As Recommended 1st line

- Benefits compared to existing regimens
- Availability
- Cost
- Pill burden - Preference for Fixed dose
- Ease of implementation
  - TB
  - Pregnant women
  - Paeds

PATIENT LEVEL BENEFITS OF TLD OVER TLE



Patients in Swaziland can benefit from clinical and convenience benefits offered by TLD

Clinical Benefit	**Superior in efficacy**	• Shown to be **superior to EFV** in multiple large phase III studies • **Faster viral suppression** in 4 weeks in TLD vs. 12 weeks in TLE
	Better tolerability	• DTG shows improved tolerability vs. current preferred regimens with substantial **reductions in treatment-limiting adverse drug reactions**
	Forgiving	• Has a **higher genetic barrier** lowering the risk of resistance from poor adherence • **No DTG INSTI resistance mutations** documented to date in treatment-naïve patients
Convenience	**Once-daily FDC & Smaller size**	• **~40% smaller pill size** (650 mg of dose in TLD vs. 1100 mg of dose in TLE)

PROGRAM LEVEL BENEFITS OF ADOPTING TLD

Cost	**Lower price than TLE**	• TLD estimated to come to market at approx. 10-15% less than prevailing TLE600 price

Cost Saving Analysis – Scenario break down for Swaziland

Scenario Comparison	2017	2018	2019	2020	2021	2022	Total
Scenario 1- No change, TLE 600 mg for ALL 1st Line Patients							
Scenario 2 - TLD for New Initiations starting 2018 + Proactive switch from TLE to TLD (full switch by 2020 – 30%, 60%, 90%)							
Scenario 3 - TLD for New Initiations starting 2019 + Proactive switch from TLE to TLD (full switch by 2021 – 30%, 60%, 90%)							
Scenario 4 - TLD for New Initiation starting 2018 + ALL switch from TLE to TLD in 2018 (full Switch by 2018 50/%, 90%)							
Scenario 5 - TLD for New Initiation starting 2019 + ALL switch from TLE to TLD in 2019 (full switch by 2020 – 50%, 90%)							

PROGRAM LEVEL BENEFITS OF ADOPTING TLD

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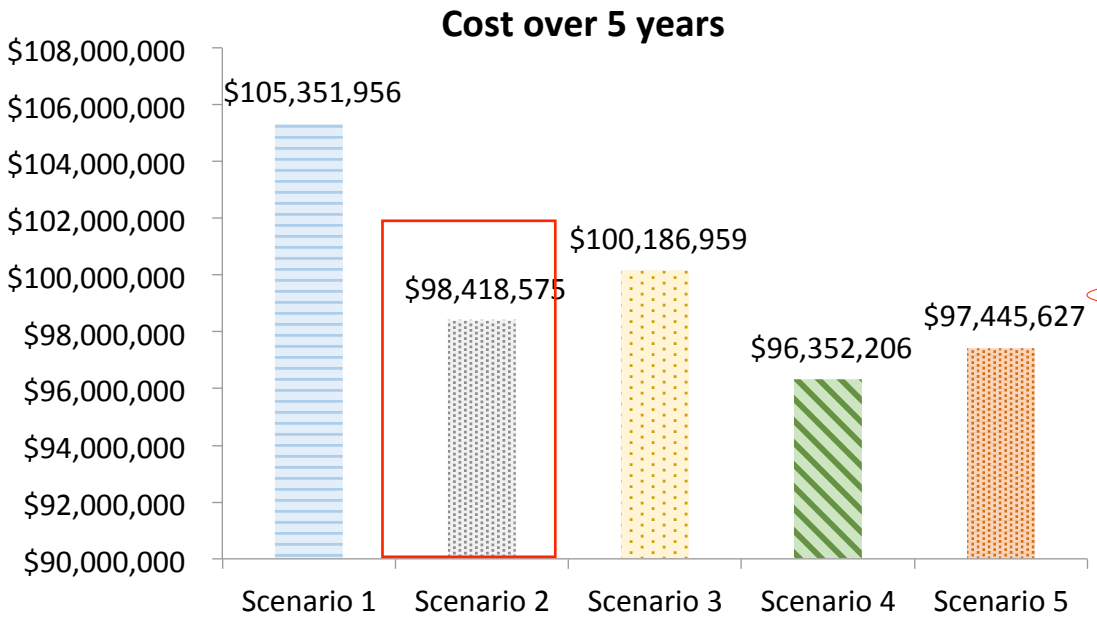


Scenario 1 -- *No Change of regimen*

Scenario 2 -- *2018 Start, Full by 2020 (phased scale- up)*

Scenario 3 -- *2019 Start, Full by 2021 (phased scale- up)*

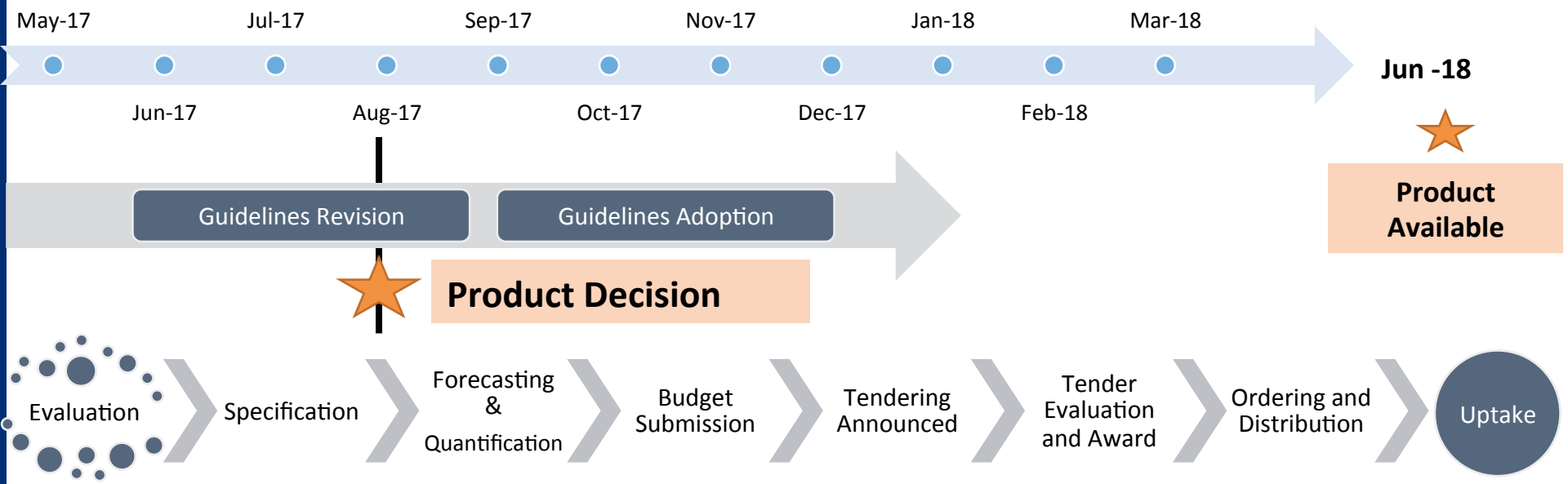
Scenario 4 -- *2018 Start, Full in 2018 (Ideal scenario)*

Scenario 5 -- *2019 Start, Full by 2020 (Aggressive scale-up)*

Faster adoption of TLD will result in faster realization of savings (adopting in 2018 vs 2019 results in almost USD 2million savings)

PROGRAM LEVEL BENEFITS OF ADOPTING TLD NOW

Availability	**At least 3 suppliers are expected to be registered to supply TLD by Q2 2018**	• Plan for Next ARV tender process • Targeting market availability Q1/Q2 2018, in time for Swaziland's next ARV tender award



To be available in 2018, the product must be adopted in the 2017 Guidelines.

PROGRAM LEVEL BENEFITS OF ADOPTING TLD NOW

TLD's adoption will not increase program complexity for SNAP

Program complexity	**Simplified regimen, and a better alternative to NVP**	**Today's regimens** TDF + 3TC + EFV AZT + 3TC + EFV TDF + 3TC + NVP AZT + 3TC + NVP **Tomorrow's regimens** **TDF + 3TC + DTG** TDF + 3TC + EFV AZT + 3TC + EFV ~~TDF + 3TC + NVP~~ ~~AZT + 3TC + NVP~~
	TB coinfection	• **1L Use:** Current guidance is to **double dose DTG** with rifampicin use - *New data expected in early 2018*
	Benefits to PMTCT	• DTG achieves **rapid viral suppression** can help PMTCT programs succeed *(Viral load at the time of delivery is the strongest predictor of transmission)* – *encouraging data at IAS 2017* • DTG can **reduce transmitted resistance**, avoiding compromising infant treatment options (NNRTI resistance is increasingly a problem for vertically infected children who are already at higher risk for treatment failure

Products Phase in/out : Lessons Learned

Experience with ;

- D4T Phase out
- Introduction of
  - TDF/3TC/EFV – Recommended first line
  - ATV/r - Recommended second line
- Other guideline changes
  - Transitioning from CD4 35-500
  - Roll out of Test and start
  - Routine Viral load

D4T Phase - out: Enablers

In 2010,

- Guidance from Program : MEMO
  - Phased roll out
- D4T Side effects profile
- Introduction of TLE fixed dose combination
  - Favored by nurses
  - Demanded by clients
- Nartis training - Substitution by Nurses
- No need for Viral load
- Mentoring

Challenges

Scale up was slow : 2010-2017

- Especially for Paeds
- No active M&E plans
  - In Sept 2014, ~ 2,500 pediatric or adolescent clients (age 0-19 years) were still on a d4T-containing regimen
  - Task team found it was largely due to data capture challenges
- Patient preference for D4T
  - Forced to switched in May 2017.

Lessons Learned from ATV/r Phase-in

In October 2015, disseminated guidelines

- all new adult and adolescent 2L clients be put on ATV/r based regimen
- However, ATV/r was not available at CMS until May 2016.
- In spite of becoming available, there was an extremely low uptake of ATV/r (<5% of the new 2L clients) and large quantity of unutilized ATV/r packs were set to expire in May 2017

ATV/r Phase-in : Barriers

- Communication
  - Time lag between guidelines dissemination and product availability
- Health care worker & mentors not trained on benefits of ATV/r Vs LPV/r
  - Efficiency
  - Side effect profile
  - cost
- Limited Monitoring of drug uptake

ATV/r Phase-in Enablers

- Collaboration with Central Medical stores team
- Sensitization meeting
  - Mentors
  - Clinicians
  - Pharmacist
- Availability of drug in facilities pharmacies
- Job aides
- Inclusion of ATV/r in essential medicines list
- Revised order book to include ATV/r
- Regular monitoring and updates

LESSONS LEARNED FROM ATV/R PHASE-IN

Second Line (2L) ART: Usage of Atazanavir/Ritonavir (ATV/r)

NOTE: ALL NEW ADULT & ADOLESCENT• 2L patients should be started on an ATV/r-containing regimen

**See opposite side for special considerations; note: adolescents must be >12 years and >40kg*

What to tell your patient?

Timing:

- Pill should be taken at the same time each day
- If you miss a dose or forget to take medicines, take it as soon as possible
- Good adherence is critical to the success of treatment; inform provider if there are barriers impacting adherence

Instructions:

- Best taken with food or milk but can be taken without; it is important to stay well hydrated to prevent kidney stones
- Do not split or crush pills
- Inform health care worker of any medications you are currently taking (see drug interactions above)

Common Side effects: *(note: all adverse events should be reported to the Pharmacovigilance Unit)*

- Jaundice – yellowing of the eyes and skin (see below)
- Allergic reaction: itching/rash
- Nausea, vomiting
- Dark colored urine or pale stools

How to monitor patients on ATV/r? (Potential Adverse Reactions)

Unconjugated Hyperbilirubinemia :

- Jaundice is a common side effect of ATV/r caused by elevated unconjugated bilirubin
- It is largely a cosmetic issue and not related to hepatitis or liver damage
- In the case of Jaundice, providers must investigate cause; blood should be taken for LFT and Hepatitis B Virus screening test
- If result of LFT indicates that AST and ALT are elevated 5 times the upper normal limit and/or patient is symptomatic and/or has Active Hepatitis B service provide should seek expert advice or switch client to LPV/r

Cholelithiasis:

- Abdominal pain
- Clients with history of kidney stones are at increased risk; clients may present with cholelithiasis and kidney stones concurrently

Other Resources:

For additional questions regarding ATV/r, refer to 2015 HIV Management Guidelines, Facility Pharmacists, your mother facility and/or regional mentors.

For stock enquiries call 2518-4111 and ask for Senior Pharmacist

For questions about paediatric care contact the Baylor Hotline: 7848-5571

Job Aid to communicate new guidelines to clinicians and pharmacists

LESSONS LEARNED FROM OTHER GUIDELINES CHANGES

- **Test and Start – National roll out**

  Enablers include;

  - Ongoing Early access to ART studies
  - Community engagement in pilot sites
  - Sensitization of all stakeholders
  - Greater involvement of PLHIV
  - Clear road map with time lines
  - Communication strategy
  - Availability of ARV supply
- **Viral Load Scale Up : Phased scale up**
  - First to children, adolescents and pregnant women, suspected treatment failure – slow then to routine monitoring

  Enablers

  - Clear road map with time lines
  - Availability of Lab supplies
  - Sensitization of network of PLHIV groups
  - Communication message
  - Support patient for demand creation
  - Fliers,Viral load stickers
  - M&E

Key processes include;

- Advocacy and stakeholder involvement
- Guidelines adoption
- Strategic planning with timelines
  - National and Facility Roll out
  - Prior and after product arrival
- Data systems
- Communication strategy
- Tools and job aides development
- Capacity building and mentoring

Central-level uptake planning and execution: Strategic planning

Approach

- **Strategy**: Ensure that there is a coordinated launch strategy in place for product roll-out, *before* the first delivery arrives in country
- **Timing**: time procurement and deliveries of new product to ensure no wastage of phased-out product
- **Supply chain and distribution considerations**
- **Phase-In Programmatic Plan**: Develop and communicate clear criteria as to which patients will be eligible for the new product. Having up-to-date patient data is critical when determining a cohort phase-in plan for the new product

Considerations

- **Despite best laid plans…:** product uptake planning must be an ongoing process. Even when advanced plans are in place, sometimes sites "don't behave" and will switch too many patients or too few (which can both have dangerous consequences).
  - Uptake must be monitored on a monthly basis

Facility-level uptake planning and execution: Facilitate product uptake

Approach

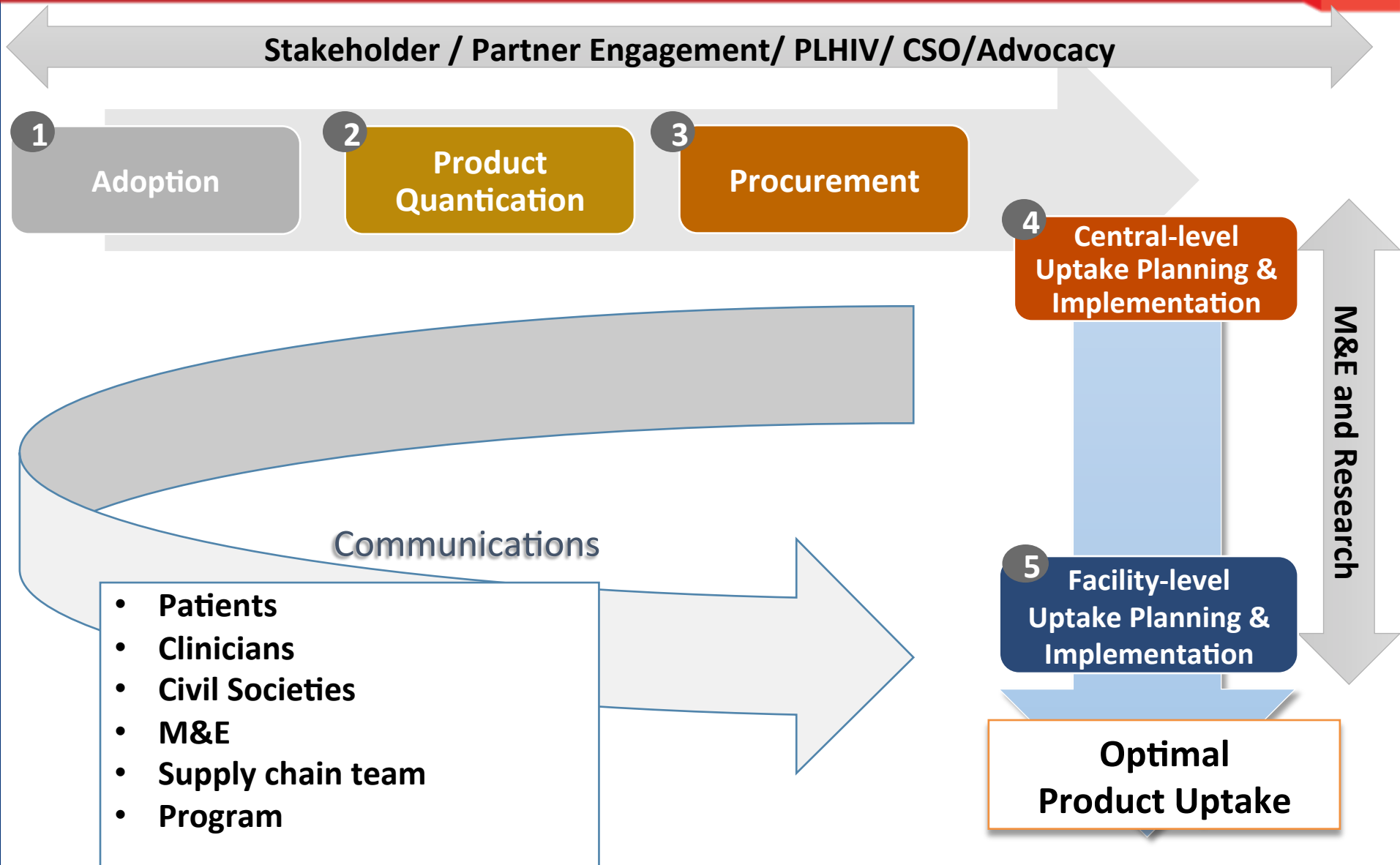
There are two distinct stages of facility-level uptake planning to consider:

- **Prior to Product Availability: Focus on Provider Education**
  - Develop job aides for sites
  - Trainings (and/or trainings of trainers)
  - Circulate memos
  - Identify potential pain points
- **Post-Product Availability: Closely monitor any uptake challenges and adapt plan accordingly**
  - Are there patient or provider acceptability issues not previously anticipated?
  - Perform site visits, revise job aides and other materials
  - Host CMEs
  - Use tools/questionnaires to collect information on uptake challenges while on site visits

Considerations

- **Partner presence:** Leveraging partners is critical when capacity is limited
- **Timing**: The trainings need to happen close to product availability, not 6-12 months before the product arrives at sites
- **Inconsistencies:** There are often significant differences between sites, depending on size, region, partners. Cannot have a one-size-fits-all approach

NEXT STEPS: AN OPERATIONAL FRAMEWORK FOR PRODUCT UPTAKE



Swaziland's Next steps

Smooth transition : April –June 2018

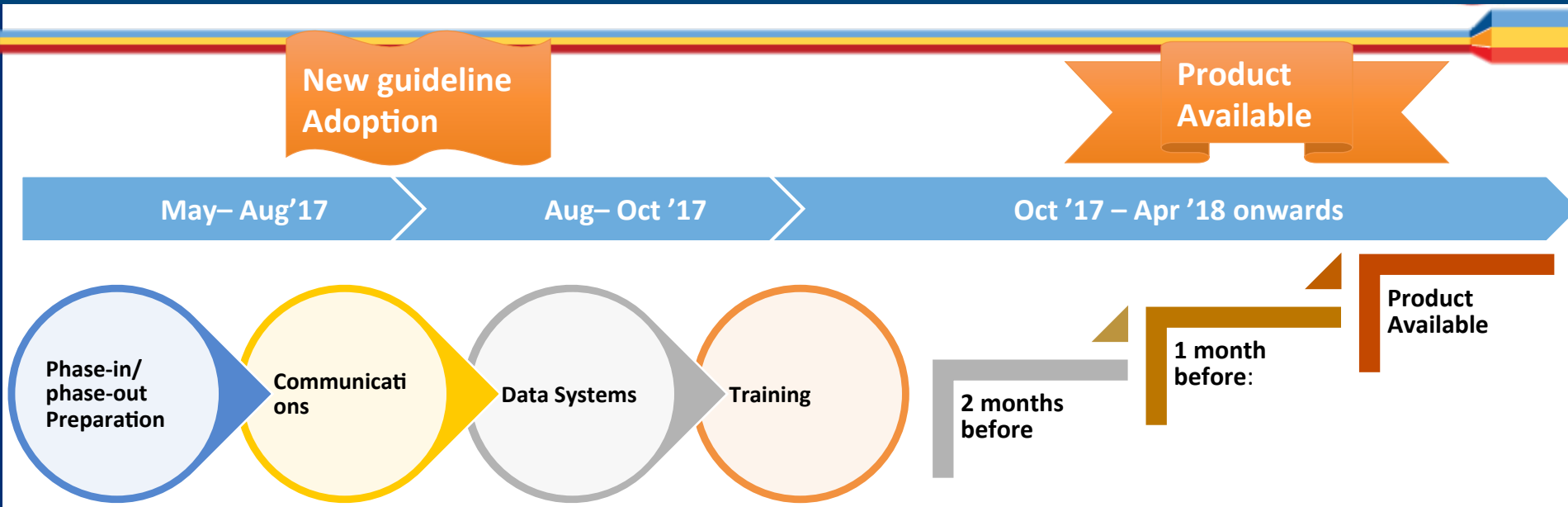
No stock wastages

Quality

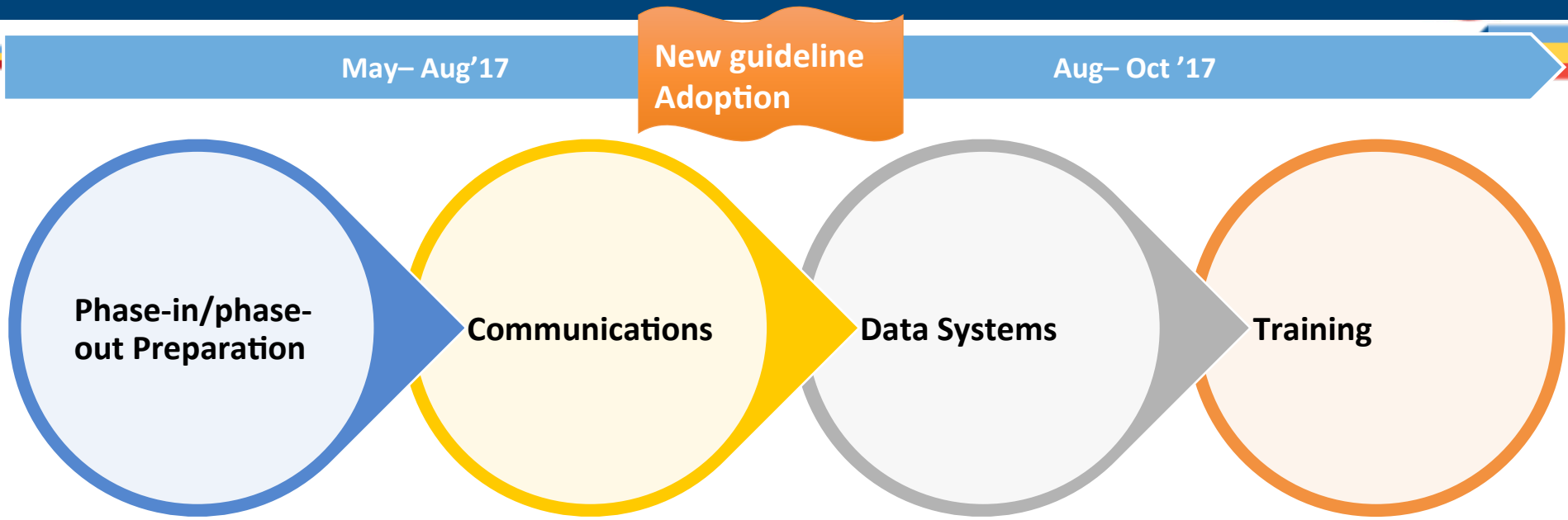
Equity

Respect for Human rights

Roadmap from Guideline Adoption to Guideline Implementation



Roadmap from Guideline Adoption to Guideline Implementation



- Quantification;
- Costing;
- Patient identification;
- Resource mapping and validation at facility level for transition prerequisite;
- Supply planning;

- Stakeholder, TWG consultations, PLHIV & civil society
- Clarify information to be communicated to whom and when;
- Develop communication strategy with timeline;

- Identify data systems to be impacted by the change in treatment guidelines;
- Update data system and data tools to incorporate upcoming products;

- Map training requirement of various stakeholders and the resources currently available;
- Develop transition algorithm;
- Identify partners for mentorship.

Roadmap from Guideline Adoption to Guideline Implementation

New guideline Adoption

Product Available

Oct ’17 – Apr ’18 onwards

2 months before:

- Partners coordination;
- Finalize algorithm;
- Data system readiness;
- Train mentors;

1 month before:

- Clarify order and delivery timeline;
- Send alert memos to facilities;
- Send transition algorithms;
- Guideline sensitization;
- Targeted training onsite;

Product Available:

- Send starter pack with confirmation memo to facilities;
- Order based on starter consumption;

- **<u>Routine:</u>**
- Onsite mentorship at facilities;
- Monitor uptake, feedback (both CMS and facilities).

ROLE OF ADVOCACY GROUPS:

- Strong Partnership collaboration with MOH to introduce DTG
- Treatment literacy for patients
  - Early information about new products
- Integration messages to existing priorities
  - Test and Start
  - Viral Load
  - Differentiated care
  - 90-90-90 - Achievement are not equally distributed among populations,
    - Adolescents lagging behind
- Advocacy for continued funding for ARVs
- Advocacy for Laboratory support
- communication strategy is key
  - Treatment optimization
  - *" Viral suppression does not mean tolerability"* - Kenly Sikwese, AfrocAB

CONCLUSION: BENEFITS OF ADOPTING DTG

- Cost savings
  - Affordable
  - Resistance barrier – patients on first line for longer
- Patient
  - Better tolerability
  - Clinical outcomes
    - Adolescents
    - Pregnant women
- Opportunities for improving
  - Treatment literacy
  - Viral load scale up
  - Test & start scale up
- Impact : 90-90-90
  - Incidence, Morbidity & Mortality

Thank you.