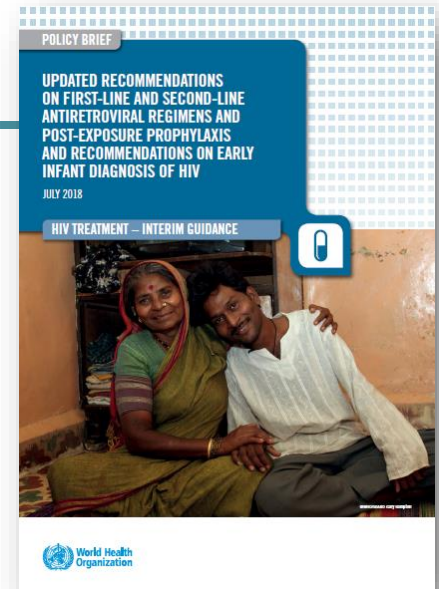




# Guideline considerations for LAIs:

How should Africa be thinking about this?

**Professor Francois Venter**  
**Ezintsha**  
**University of the Witwatersrand**  
**Johannesburg, South Africa**





## Disclosures: Francois Venter

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Speaker's Bureau/Board Member/Advisory Panel: Gilead, ViiV, Mylan, Merck, Adcock-Ingram, Aspen, Abbott, Roche, J&J, Sanofi and Virology Education. Southern African HIV Clinicians Society



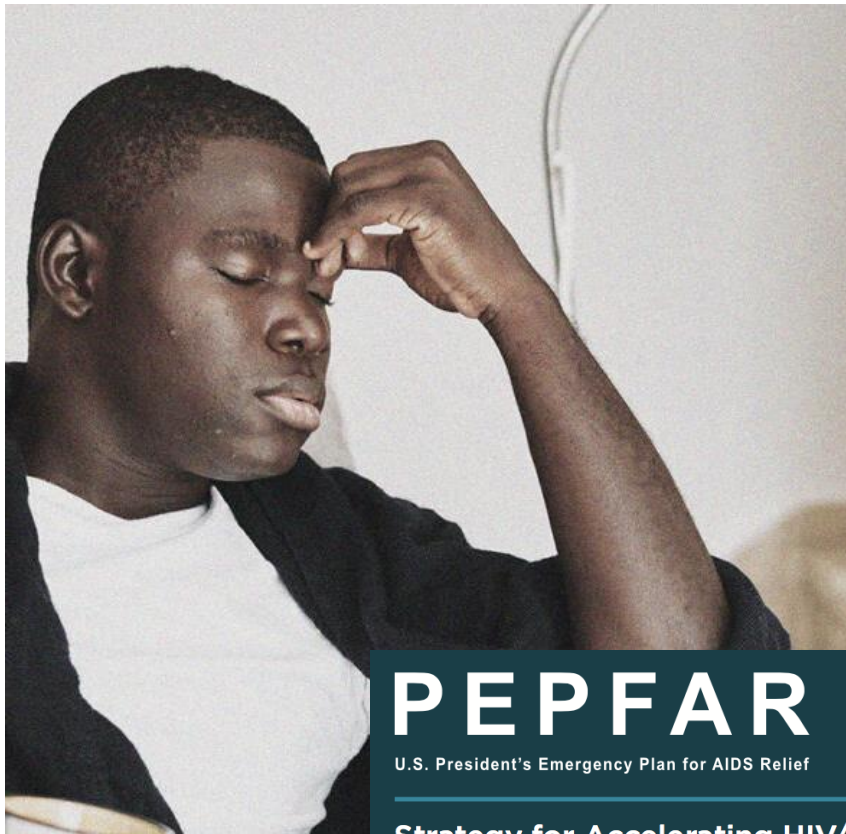
# Guidelines are critical to getting access

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- **No guideline = no demand = no generics = no cost reduction**
- **South Africa especially critical – 20% generic ARV market**
- **Also critical is PEPFAR: similar large procurer**

# Why are injectables likely to be harder?



**PEPFAR**

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

Strategy for Accelerating HIV/AIDS  
Epidemic Control (2017-2020)

- **Manufacturing cost is much higher than for oral agents – hence generics are going to need high-level certainty**
  - Guideline alignment
  - Early adoption – SA, large donors like PEPFAR critical
  - ?Volume guarantees
  - Generics burnt before (EFV 400mg, paediatric formulations)

# Then y'all better make up your minds! (WHO and SAHCS not a priority for originators)

C. Flexner, A. Owen, M. Siccardi et al.

International Journal of Antimicrobial Agents 57 (2021) 106220

**Table 1**

Long-acting drugs in development for human immunodeficiency virus (HIV) prevention (Px) and treatment (Tx) by infusion, injection or implant.

Antiretroviral class/agent	Formulation	Development stage
Nucleoside reverse transcriptase inhibitors (NRTI)		
Islatravir (MK-8591)	Implant/Oral	Phase 1/2 (Px)
TAF	Implant	Phase 1/2 (Px)
GS-9131	Implant	Preclinical
Non-nucleoside reverse transcriptase inhibitors (NNRTI)		
Rilpivirine	Injectable	Phase 3/NDA
Elsulfavirine	Injectable	Preclinical
Protease inhibitors (PI)		
Atazanavir	Injectable	Preclinical
Ritonavir	Injectable	Preclinical
Integrase strand transfer inhibitors (INSTI)		
Cabotegravir	Injectable	Phase 3/NDA, phase 2/3 (Px)
Dolutegravir	Implant	Preclinical (Px)
Raltegravir	Injectable	Preclinical
Entry inhibitors		
Ibalizumab	Intravenous	FDA-approved (Tx)
Leronlimab (PRO 140)	Intravenous and Injectable	Phase 3
Albuvirtide	Intravenous and injectable	Approved in China
bnAbs (e.g. VRC01, VRC07)	Intravenous	Phase 1/2/3
Combinectin	Intravenous	Phase 1
Capsid inhibitors		
Lenacapavir (GS-6207)	Injectable	Phase 2

NDA, New Drug Application; FDA, US Food and Drug Administration; bnAbs, broadly-neutralising antibodies.



Shout out... <https://i-base.info/>

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# HIV pipeline 2021

htb supplement: 2021 Vol 22:(1), August 2021

New drugs in development

## CONTENTS

### HIV pipeline 2021: targets in the HIV lifecycle

**NRTIs/NRTTIs (nukes)**  
efavirenz (EFV)

**Monoclonal antibodies (mAb)**  
UB-421 (CD4 scavenger)  
VRC01/LS and VRC07/LS  
SNC117/LS and 10-1074/LS  
PGDM140, 10E8.4/mAb  
PGT-21 and elvitegravir (as part of NLS)  
lenalimumab (PRC-140)

**Stages in the HIV lifecycle:**

- 1 HIV attaches to a CD4 cell
- 2 HIV enters a CD4 cell and the capsid is released into the cell
- 3 The capsid enters the cell nucleus where HIV proteins and enzymes are released.
- 4 Reverse transcriptase (RT) makes double strand HIV
- 5 Integrase enables HIV DNA to join the cell DNA.
- 6 New viral material is made.
- 7 Proteases cure and recombine new HIV.
- 8 Each cell produces

# WHO considerations

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- **Cost**
- **SA=Malawi=Spain**
- **Implementation – a big deal here: injection sites, co-formulations**
- **Pregnancy, mother-to-child-transmission**
- **Resistance – tests available in rich countries, N/A even in SA**
- **Transference between paed populations and adults**
- **Drug-drug interactions (esp TB)**
- **Other:**
  - Hepatitis B (esp TDF/TAF), C
  - Advanced disease



# South African considerations – SAHCS role vs DoH

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- **Public vs private**
- **Tenders are complex in terms of timing**
- **Medical aids**



# Scenario A: eg rilpivirine/CAB for treatment

## FDA Approves 1st Long-Acting HIV Drug Combo, Monthly Shots

U.S. regulators have approved the first long-acting drug combo for HIV: monthly shots that can replace daily pills.

By Associated Press, WebMD Health Content. Apr 21, 2021, 4:17 PM



- **Expensive! Very, very unlikely to = 1<sup>st</sup> line TLD**
- **Cold chain, 2 separate complex injections, ?genotyping**
- **Medical aids: will balk**
- **SAHCS – going to be hard to recommend outside of a ‘consider’**
- **DoH: ? For niche groups**
- **BUT: what if price drops – and shown to work in certain groups eg: adolescents**
- **Huge pushback already PEPFAR and governments – decentralized programmes “undermined”**

## Scenario B: Originator cabotegravir PrEP

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- **Access pricing for DoH, confusing situation private (let's assume significantly more expensive)**
- **SAHCS: Hard! Better drug but much more expensive – but private programme a disaster, public programme not much better**
- **DoH: Taken a long time to tick the 'most sites' box – now an injectable?**

# Scenario C: Generic cabotegravir

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- **CHAI: same cost as oral PrEP (not including the HCW costs)**
- **Thorny – throws a microscope on how bad the PrEP programme is overall**
- **Who DON'T you give it to?**
- **Why aren't medical aids falling over themselves to provide it?**
- **Where will mass injection sites be?**

# My take

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- **LAI**s tremendously exciting – but they pose significant guideline challenges
- **BUT** we have some time to crack these
  - Not unsolvable – start trying some creative ideas
  - Will be some time before mass availability
- **Patients** may push us very hard and fast
- **PrEP** cabotegravir will be the big initial tester