Ethics of Post Research Responsibilities and obligations: The Past and Present, Areas of Agreement and Controversies; Next steps for Uganda and the Region

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UNCST

MU-JHU

Outline

- Why PRR Matters: The Ethical Imperative
- The Evolution of PRR: Past and Present
- Areas of Agreement and Core Controversies
- Next Steps for Uganda and the Region
- Case studies of PrEP trials in Uganda
- Conclusion and Call to Action

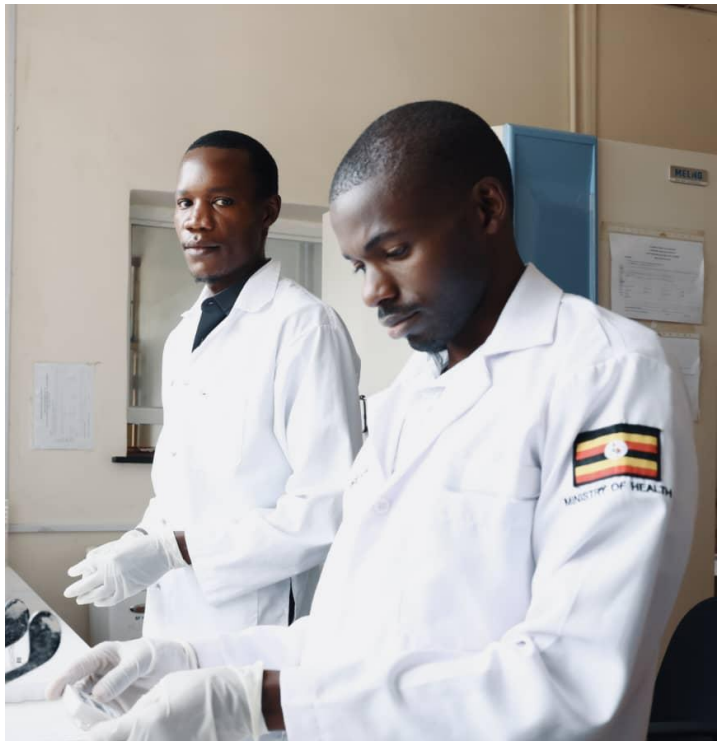
Why PRP Matters: The Ethical Imperative

The Paradox of Progress

- We celebrate successful trials (e.g., HIV treatment, PrEP,), but a profound ethical question remains:

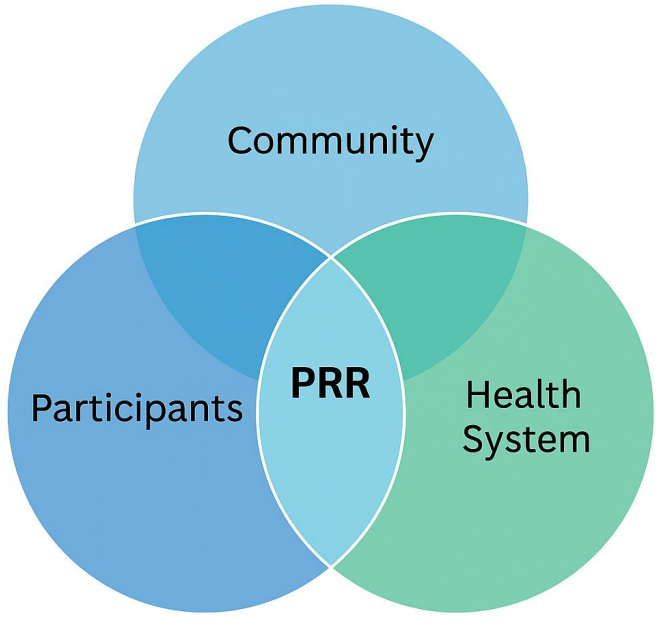
  "What happens when the protocol ends and the sponsor leaves?"

- Our research success creates a moral debt



Defining PRR

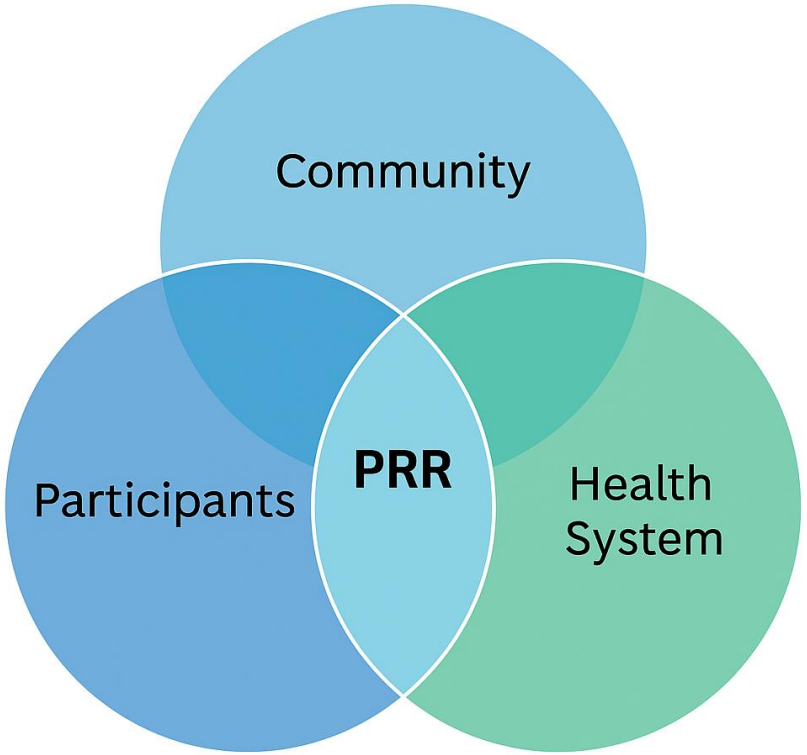
- Obligation owed to participants, communities, and health systems after the formal study intervention/data collection is complete
- Ethical drivers: Beneficence, Non-maleficence, and Justice
- It encompasses the moral and practical duties that extend beyond study closure, covering:
  - Post-trial access
  - Ancillary care, and
  - Sustainable capacity Building
- Research is a **social contract**. PRR ensures this contract is honored



Why PRR?

- **PRR** is central to Responsible Conduct of Research and ensuring research impact and equity in Africa

- **Focus Areas:** Access to study interventions, community feedback, long-term care, capacity building sustainability, and publication/ dissemination



The Evolution of PRR: Past and Present

PRR: The Past - Historical Underpinnings

- Research was often extractive, leaving communities with little more than the knowledge generated
- Despite active participation and contribution to the research, participants were unable to access/ afford the product once the study ended
- PRR often vague, non-binding, or non-existent in protocols for resource-limited settings

PRR: Tracing the Ethics of Obligation

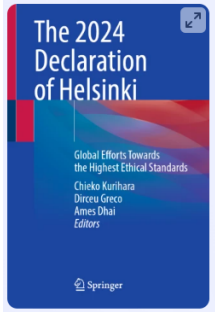
- **The Early Era (Pre-2000s):** Focused primarily on **immediate participant safety** and reporting.
  - **Nuremberg Code (1947) & Declaration of Helsinki (1964):** Focused primarily on participant protection during the research
  - **The Belmont Report (1979):** Introduced **Beneficence** and **Justice**, which lay the groundwork for PRR (e.g., maximizing benefits and fair distribution of research burdens/benefits)

The Turning Point: Declaration of Helsinki **2000 & 2013**

- **Key Milestones:** The 2000 revision of the Declaration of Helsinki (DoH) was revolutionary, initially demanding participants be "assured of access.“
- This was softened to **"reasonable availability"** in the 2013 revision (Para 34)
- **The Shift:** Moving from simply preventing harm to actively **promoting sustained good**
- This **shift defined the modern debate**, acknowledging that access requires practical planning

The Present: Formalizing PRR - International Guidelines

- **Core Mandates**
  - **WMA Declaration of Helsinki**
  - **CIOMS/WHO CIOMS Guidelines**



The 2024 Declaration of Helsinki

Global Efforts Towards the Highest Ethical Standards

Book | © 2025

CIOMS (Council for international Organizations of Medical Sciences)

Declaration of Helsinki (World Medical Association)

2024 Declaration of Helsinki, article 18:

(Emphasizes post-trial access to proven interventions)

> *"Every research should include provisions for **post-trial access** to interventions identified as beneficial in the study or access to other appropriate care. This provision should be made known to the participant during the informed consent process."*

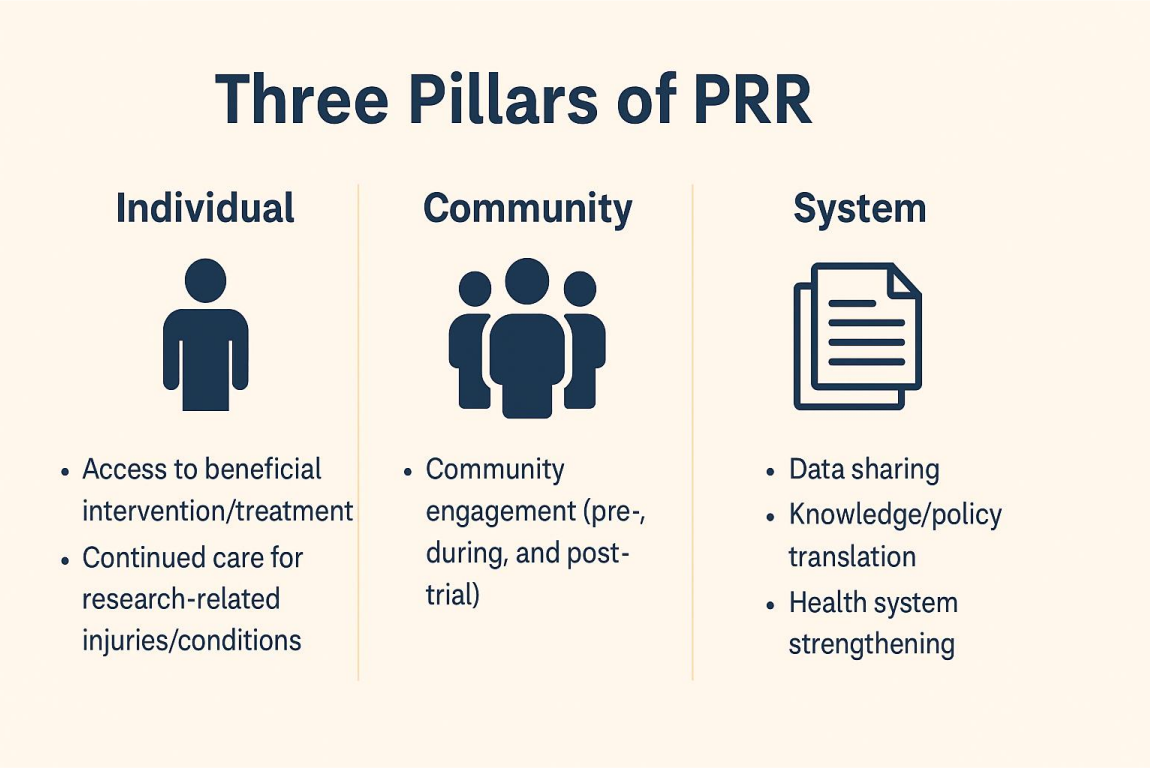
CIOMS Guidelines (CIOMS/WHO) 2016

- **Availability of beneficial intervention for participants and sustainable measures for community benefit:**

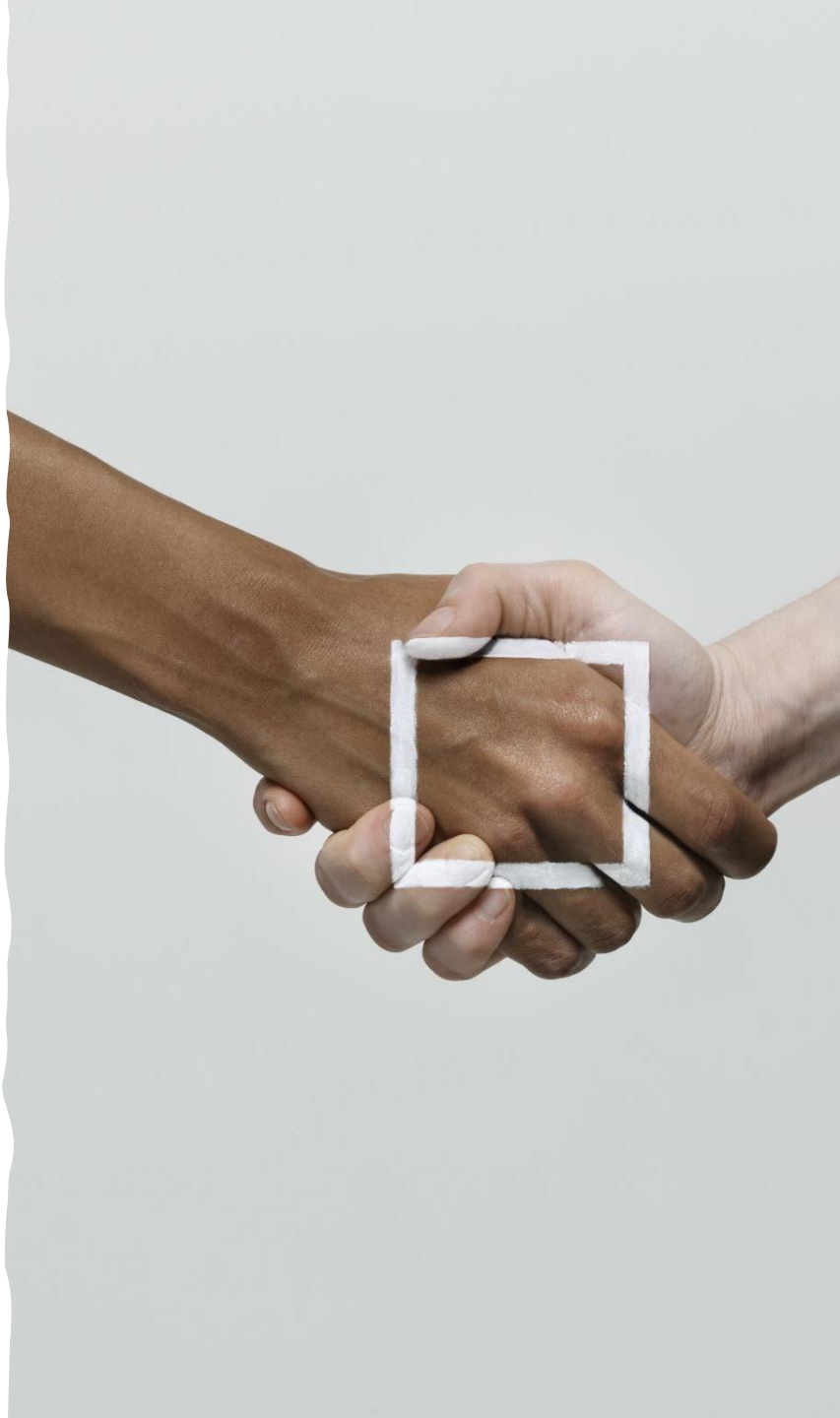
  A. Availability of Beneficial Interventions (Guideline 2)

  B. Caring for Participants' Health Needs (Guideline 6)

PRR Scope


Three Pillars of PRR
Individual
Access to beneficial intervention/treatment
Continued care for research-related injuries/conditions
Community
Community engagement (pre-, during, and post-trial)
System
Data sharing
Knowledge/policy translation
Health system strengthening

Areas of Agreement and Core Controversies



Consensus

- **Community Engagement:** Researchers must involve communities in planning and dissemination
- **Transparency:** Ethical research requires clear communication of goals, risks, and outcomes to build trust
- **Capacity Building:** Strengthening local research infrastructure/ skills is a shared responsibility
- **Access to Benefits:** Participants should benefit from research findings/ interventions

Area of controversy 1: What is reasonable?

- Does "access" mean free access, subsidized access, or simply making it available in the market? For how long?

Areas of controversy 2: Individual vs. System PRR

- Should PRR be limited to ensuring individual participants receive the intervention, or does it include a broader obligation to communities, and to local health systems strengthening?

- ***The African Context: System-level PRR (e.g., upgrading labs, training personnel) is often argued as one of the most meaningful form of lasting benefit***

Areas of controversy 3: Funding

- Who is primarily responsible for long-term access to a proven beneficial intervention (e.g., a new PrEP formulation or HIV regimen) after the trial concludes?

- Is the Sponsor/funder solely responsible, or does the host government/Ministry of Health share the burden?

Areas of controversy 4: Sustainability

- For how long should post-trial access continue

If you agree for your child to take part in this study, your child will receive the study medication(s) until they turn 18 years old, or for up to 1 year if your child is already 17 years old. During the study, your child will also come to the study site regularly for monitoring, such as measurement of body weight, to answer questions about how they are feeling and review their current study medication(s) and other medications.

Controversy 5: Ancillary Care (The Scope of Duty)

- What is the scope of obligation for follow-up care for conditions unrelated to the study intervention but discovered during the trial (e.g., hypertension discovered during an HIV study)?

- The Partial Entrustment Model suggests a temporary moral obligation to address urgent health needs through clear referral pathways.

Controversy 6: Beyond Interventions - Data and Specimens

- **Data:** How do we ensure data is shared responsibly, and ethically with local researchers

- **Specimens:** Who owns them? Where are they stored? How do we ensure long-term benefit and accessibility for future local research

Common objections against post-trial access

- PTA may cause undue inducement, since the expectation of follow-up care or any other benefit, especially in resource limited settings, may persuade people to participate in clinical trials
- PTA may delay trials because of procedures and agreements to be made with sponsors, and researchers, and governments
- PTA may prevent trials happening, since the final financial burden of PTA provision may become a disincentive for sponsors to conduct clinical trials in resource limited settings
- PTA may be misused as a marketing tool

Current Status of PRR in Uganda and the Region

The Ugandan Landscape: Progress and Challenges

- **Progress:**
  - Strong regulatory bodies (UNCST, NDA) and accredited RECs
  - Growing focus on PRR clauses in local guidelines (e.g., National Guidelines for Research)
- **Challenges:**
  - Enforcement of PRR clauses
  - Ensuring policy uptake post-research
  - Dependency on external funding

The Role of Local Research Institutions

- **Local PIs/Institutions are the PRR Stewards and are responsible for:**
  - negotiating robust PRR terms; advocate for participants
  - ensuring sustained capacity building efforts
  - serving as the link between international partners and the host community/system
  - disseminating research findings and advocating for policy change

Research to policy - ? practice

Groups at Risk of developing Low Bone Mineral Density on TDF

1. **Women using Depo-Provera** for contraception on TDF (**concomitant use of Depo-Provera results in a doubling of BMD loss in women living with HIV initiating TDF-containing ART)**. Intramuscular depot medroxyprogesterone acetate accentuates bone loss associated with tenofovir disoproxil fumarate-containing antiretroviral therapy initiation in young women living with HIV (the BONE: CARE study): a prospective cohort study in Uganda - The Lancet Global Health
2. Peri/post-menopausal women due to the hypoestrogenic state – women about the age of 45 and above HIV and Bone Health: Considerations for Menopausal Women Living with HIV in Sub-Saharan Africa | Journal of Bone and Mineral Research | Oxford Academic (oup.com)
3. Children and adolescents as these have not yet attained their peak bone mass noting that peak bone mass determines one's risk of fractures later on in life.
4. Breastfeeding women (Study demonstrated that in Ugandan women living with HIV who initiated TDF during pregnancy, bone loss during lactation was exacerbated compared with controls, and the usual recovery of bone after weaning did not occur. https://asbmr.onlinelibrary.wiley.com/doi/full/10.1002/jbmr.4121).

What risk groups are to be targeted?

What is the implication of this on the current HIV guidelines?

Current guideline recommend TDF-3TC-DTG as the preferred regimen for children and adolescents.

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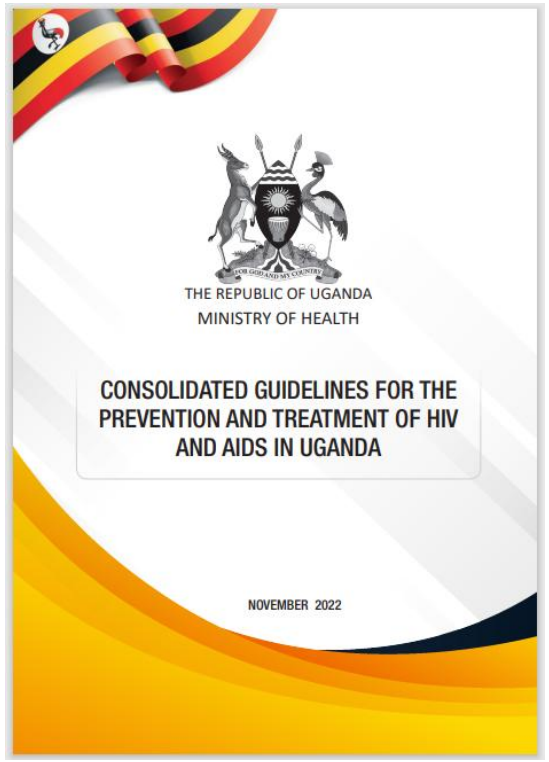

Chapter 7: TB 74: Recommended first-line ARV regimens in Children, adolescents, adults and pregnant or breastfeeding women

Adults and adolescents ≥ 30Kg	TAF + FTC + DTG or TDF + 3TC + DTG	Pregnant and breastfeeding women: TDF + 3TC + EFV400 or TAF + FTC +EFV400 If DTG is contraindicated1: TDF + 3TC + EFV400 or TAF + FTC +EFV400 If TDF or TAF is contraindicated2: ABC + 3TC +DTG If both TDF or TAF and DTG are contraindicated: ABC +3TC +EFV400 If EFV and DTG are contraindicated: TDF +3TC + ATV/r or TAF + FTC +ATV/r or ABC + 3TC + ATV/r
Pregnant and breastfeeding women	TAF +FTC + DTG or TDF +3TC+ DTG	
Children ≥20Kg- <30Kg	ABC + 3TC + DTG or TAF +FTC + DTG	If DTG is contraindicated: ABC + 3TC + LPV/r (tablets) If ABC is contraindicated: AZT + 3TC + DTG or TAF + 3TC + DTG (TAF in children> 6 years and ≥25Kg)
Children <20Kg	ABC + 3TC + DTG	If intolerant or appropriate DTG formulations are not available: ABC +3TC + LPV/r (syrup, pellets, or tablets). If intolerant to LPV/r: ABC + 3TC + EFV (in children > 3 years and >10Kg) If ABC is contraindicated: AZT + 3TC + DTG or LPV/r

6

Regional Perspectives: Shared Responsibilities in East Africa

Similar challenges across the region (Tanzania, Kenya, Rwanda):

- High research volume
- Resource-limited settings, and
- Consistent struggle to translate research success into lasting public health gain

Need for Regional Harmonization: Common standards for PRR across EAC research consortia

Platforms like AccessAfrica2 and AVAREF enable shared standards and joint ethical reviews for multi-country research studies

Case studies - PrEP trials (Results to Clinic)

Comparison of Key Access Milestones for PrEP trials

Milestone	Daily Oral PrEP (TDF/FTC)	Dapivirine Vaginal Ring (Monthly)	CAB-LA Two-monthly Inj.	Lenacapavir (LEN)-Twice Yearly Inj.
Phase III Efficacy Results Release	**2010/2011** (iPrEx, Partners PrEP, TDF2 trials)	**February 2016** (ASPIRE & Ring Study results)	**May 2020** (HPTN 083/084 interim results)	**June 2024** (PURPOSE 1/2 interim results)
Major Regulatory Approvals (US/EU)	**July 2012** (US FDA approval for Truvada for PrEP)	**July 2020** (EMA Positive Opinion for RLS use)	**December 2021** (US FDA approval for Apretude)	**June 2025** (US FDA approval for Yeztugo)
WHO Recommendation/ Prequalification	**2012/2015** (Initial guidance on demonstration projects; strong recommendation by 2015)	**January 2021** (Conditional Recommendation/Prequalification)	**2023** (WHO Prequalification/Guidance)	**July/Oct 2025** (Guidance & Prequalification)
Uganda NDA Registration	**Pre-2017** (Generic TDF/FTC registration was largely streamlined as an existing ART)	**October 5, 2021** (Formal NDA Registration)	**2024** (National Drug Authority approval)	**Late 2025 / Early 2026** (Projected)
Uganda National Rollout/ Pilot Start	**Late 2025 / Early 2026** (Projected)	**Late 2022 / Early 2023** (Pilot implementation studies began at select facilities)	**Late 2024 / Early 2025** (Targeted implementation start)	**2026** (Targeted National Introduction via PEPFAR/Global Fund)
Current Status	**Widespread Availability** (Implemented across hundreds of facilities)	**Limited Availability** (Available at 7 facilities in 2024, expanding slowly)	**Pipeline / Initial Implementation** (Targeting 7-11 facilities by early 2025)	**Accelerated Pipeline** (Awaiting in-country registration & delivery system setup)
Lag Time	**Oral PrEP: 5-6 years**	**DVR: 7 years**	**CAB-LA: 5 years**	**LEN: < 2 years** (Projected)

Twice-yearly injectable Lenacapavir for PrEP: fast-tracked

- Extensive community engagement – global community advisory board and in-country CAB members
- Dedicated budget for community engagement

- Study design
  - Open label extension phase included in main protocol

  - Post-trial access guaranteed until the product is publicly available in Uganda and South Africa

PURPOSE 1 Global community engagement meeting – Kigali, Rwanda, Dec 2019

Results dissemination and advocacy

Twice-yearly injectable Lenacapavir – Key milestones

MENU

GILEAD

Press Releases

June 20, 2024

Gilead's Twice-Yearly Lenacapavir Demonstrated 100% Efficacy and Superiority to Daily Truvada® for HIV Prevention

– First Phase 3 HIV Prevention Trial Ever to Show Zero Infections –

– Independent Data Monitoring Committee Recommended That Gilead Stop the Blinded Phase of the PURPOSE 1 Trial at Interim Analysis and Offer Open-Label Lenacapavir to All Participants –

Foster City, Calif. – June 20, 2024 – Gilead Sciences, Inc. (Nasdaq: GILD) today announced topline results from an interim analysis of its pivotal, Phase 3 PURPOSE 1 trial indicating that the company's twice-yearly injectable HIV-1 capsid inhibitor, lenacapavir, demonstrated 100% efficacy for the investigational use of HIV prevention in cisgender women.

PURPOSE 1 met its key efficacy endpoints of superiority of twice-yearly lenacapavir to

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

L.-G. Bekker, M. Das, Q. Abdool Karim, K. Ahmed, J. Batting, W. Brumskine, K. Gill, I. Harkoo, M. Jaggernath, G. Kigozi, N. Kiwanuka, P. Kotze, L. Lebina, C.E. Louw, M. Malahleha, M. Manentsa, L.E. Mansoor, D. Moodley, V. Naicker, L. Naidoo, M. Naidoo, G. Nair, N. Ndlovu, T. Palanee-Phillips, R. Panchia, S. Pillay, D. Potloane, P. Selepe, N. Singh, Y. Singh, E. Spooner, A.M. Ward, Z. Zwane, R. Ebrahimi, Y. Zhao, A. Kintu, C. Deaton, C.C. Carter, J.M. Baeten, and F. Matovu Kiweewa, for the PURPOSE 1 Study Team*

ABSTRACT

BACKGROUND

There are gaps in uptake of, adherence to, and persistence in the use of preexposure prophylaxis for human immunodeficiency virus (HIV) prevention among cisgender women.

METHODS

We conducted a phase 3, double-blind, randomized, controlled trial involving adolescent girls and young women in South Africa and Uganda. Participants were assigned

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US FDA approves Gilead's twice-yearly injection for HIV prevention

Thursday, June 19, 2025

Gilead Sciences in Oceanside, California, U.S., April 29, 2020. PHOTO/ REUTER

By Reuters
News agency
Thomson Reuters

What you need to know:

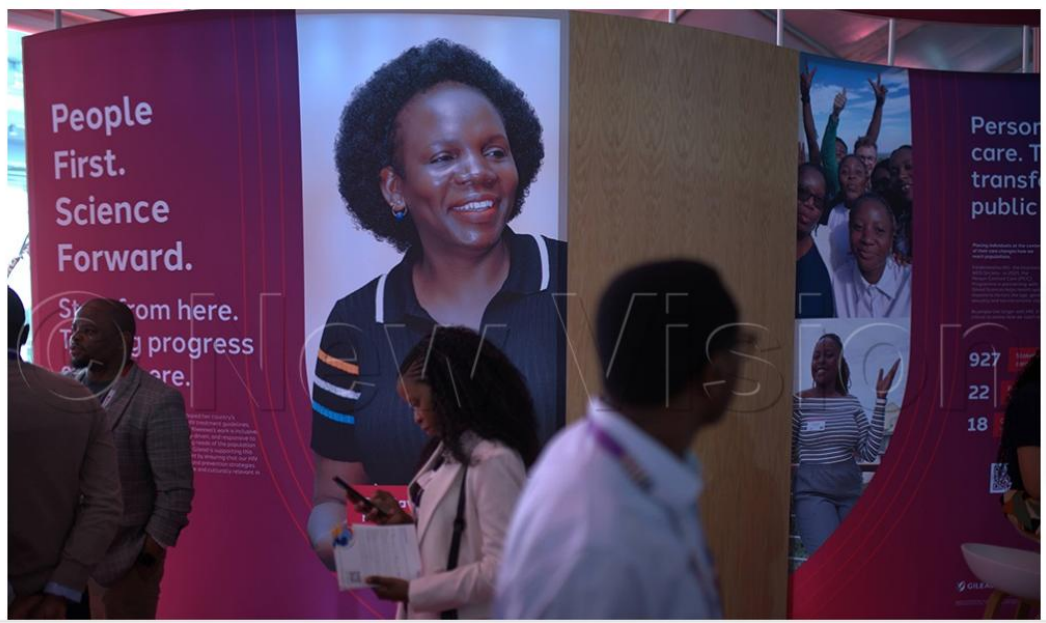
- Investors and AIDS activists had been eagerly awaiting the regulatory decision for a drug some have said could help end the 44-year-old HIV epidemic.

Health

WHO recommends Uganda-tested HIV prevention drug, issues guidelines on usage

The recommendation comes just weeks after the US Food and Drug Administration (FDA) approved the drug for use. Lenacapavir trials were conducted in Uganda and South Africa and demonstrated 100% protection, making it the most effective scientific breakthrough in HIV prevention to date.

17th July 2025 116 views



Access plans for Lenacapavir

- Gilead Sciences Inc.
  1) Signed voluntary licensing agreements with five generic manufacturers to expedite access to LEN in high incidence RLS
  2) Ensured dedicated supply in the countries where need is greatest until voluntary licensing partners are able to supply high-quality, low-cost versions of LEN
     - Global fund has donated 36,000 doses of LEN to Uganda MOH cover expected to cover 19,000 peoples starting 1st quarter 2026
     - US government has committed to purchasing lenacapavir for up to 2 million individuals in 10 HIV high burden settings including Uganda by 2028


U.S. EMBASSY UGANDA ANNOUNCES INTRODUCTION OF LENACAPAVIR, A GROUNDBREAKING HIV PREVENTION MEDICINE, DEMONSTRATING AMERICAN EXCELLENCE IN SCIENCE AND AMERICAN LEADERSHIP IN HIV PREVENTION

Press Release

Kampala, September 30, 2025 –

The U.S. Department of State announced a life-saving development to bring U.S.-based Gilead Sciences' breakthrough drug lenacapavir to market in Uganda, one of just ten high-burden HIV countries where the drug will be distributed through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). The U.S. initiative – which will promote global scale in production and distribution of the medication and catalyze further global investment has the potential to save hundreds of thousands of lives.

The United States, in collaboration with the Ugandan Ministry of Health, will introduce lenacapavir in 2026. Taken only twice a year, lenacapavir offers a highly effective and convenient HIV prevention option for individuals at high risk of HIV acquisition. Clinical trials show more than 99% of people on lenacapavir remained HIV negative.

This innovative medication represents a significant advancement in Uganda's fight against HIV/AIDS, particularly for pregnant and breastfeeding mothers. The U.S. government and the Global Fund, of which the U.S. government is the largest donor, are co-funding this advanced market commitment to purchase lenacapavir for up to 2 million individuals by 2028 in countries with the largest HIV/AIDS epidemics. Gilead has agreed to provide the drug at cost. In addition, Gilead has agreed to provide their intellectual property to generic manufacturers who can

Next Steps for Uganda and the Region

A pragmatic 5-point plan for a more ethical research future

1

Mandate Pre-Trial Agreements : Make the PTA a non-negotiable requirement for REC approval

2

Cost of PRR in Budget: Require sponsors to ring-fence a percentage of the total grant for post-study transition/handover

3

Strengthen REC Oversight: ECs to rigorously review PRR clauses for feasibility and sustainability

4

Policy Translation Track: Establish a clear mechanism(MoH) for rapid evaluation and integration of successful trial results into national guidelines

5

Community involvement: Fosterin g community engagement and advocacy to ensure research benefits meet local needs

Conclusion and Call to Action

- PRR is the essential bridge between scientific discovery and social benefit. It demands: **Partnership**, **Justice**, and **Sustainability**
- PRR is an **investment in trust** with communities, **sustainability** of health gains, and **equitable partnership** with the global research community
- Pre-trial access is a non-negotiable requirement including **ring-fenced funding for post-study transition**
- Need to **establish a rapid policy translation** track to convert successful research findings into guidelines
- Let us ensure that **no participant ever leaves** a successful trial **without access to the product** they helped discover

"A true mark of ethical research is not just what's achieved during the study, but what remains after it ends."

Anonymous

Acknowledgements

- Participants and their communities
- Study sponsors
- Research institutions/ Investigators
- Community Advocates
- UNCST, NDA, RECs
- MOH
- Uganda AIDS commission
- ANREC Organizers

Thank you!