CLASSIFICATION OF HIV PREVENTION TOOLS, THEIR ACCESSIBILITY, AVAILABILITY, AND AFFORDABILITY

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aidsfonds

KELIN
Reclaiming Rights, Rebuilding Lives

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Every effort has been made to verify the accuracy of the information contained in this report. All information was believed to be correct as of October 2023. Nevertheless, KELIN cannot accept responsibility for the consequences of its use for other purposes or in other contexts.

Disclaimer

The findings and recommendations in this report do not necessarily represent the views of the organizations involved or their respective management teams.

Abbreviations

AGYW	Adolescents Girls and Young Women
AIDS	Acquired Immune Deficiency Syndrome
ARIPO	African Regional Intellectual Property Office
ARV	Antiretroviral
CAB-LA	Cabotegravir Long-Acting
CROI	Conference on Retroviruses and Opportunistic Infections
CSO	Civil Society Organization
DVR	Dapivirine Vaginal Ring
EAC	East Africa Community
EMEA	European Medicines Agency
EU	European Union
EU-M4All	European Union – Medicines for All
F/TAF	Emtricitabine / Tenofovir Alafenamate
FDA	Food and Drug Administration
FF	Fisherfolks
FSW	Female Sex Workers
HIV	Human Immunodeficiency Virus
HIVR4P	HIV Research for Prevention
IAS	International AIDS Society
ICASA	International Conference on AIDS and STI in Africa
IDU	Injection drug users
IP	Intellectual Property
IPD	Intellectual Property Rights
KAIS	Kenya AIDS Indicator Survey
KDHS	Kenya Demographic and Health Survey
KEMSA	Kenya Medical Supplies Agency
KENPHIA	Kenya Population-based HIV Impact Assessment
KIPI	Kenya Industrial Property Institute
KPPB	Kenya Pharmacy and Poisons Board
LDC	Least Developed Countries
LIC	Low-Income Countries
LMIC	Lower-Middle Income Countries
MAGHP	Marketing Authorization for Goal Health Products
MoH	Ministry of Health
MSM	Men who have sex with men
NACC	National AIDS Control Council
NASCOP	National AIDS and STI Control Program
NRA	National Regulatory authorities
PDP	Product Development Partnerships
PEP	Post Exposure Prophylaxis
PEPFAR	President's Emergency Plan for AIDS Relief
PLWH	People Living with HIV
PrEP	Pre-Exposure Prophylaxis
R&D	Research and Development
SRA	Stringent Regulatory Authorities

SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infections
TasP	Treatment as Prevention
TDF	Tenofovir Disoproxil Fumarate
TRIPS	Trade-related aspects of Intellectual Property Rights
UNAIDS	United Nations
USAID	US Agency for International Development
WHO	World Health Organization
WTO	World Trade Organization

EXECUTIVE SUMMARY

Kenya is a high HIV burden country, with an estimated 1.5 million people living with HIV and 36,000 new infections annually. Despite tremendous efforts to curb the epidemic, a significant proportion of the population remains at risk. Effective combination prevention is needed to drive towards zero HIV infections and curb the epidemic by 2030. The government currently provides oral pre-exposure prophylaxis (PrEP) at public health facilities, but novel HIV prevention methods such as cabotegravir injection (CAB-LA) and the dapivirine vaginal ring (DVR), offer alternative acceptable, discrete and convenient choices for highly effective HIV prevention. CAB-LA is superior to oral PrEP, and DVR offers choice for women. Both products have been approved in some countries but remain inaccessible to most individuals at risk in Kenya.

We reviewed HIV prevention interventions with the aim of classifying available tools and investigating barriers to their availability, accessibility, and affordability in Kenya. Key findings include:

i. Richness of HIV prevention pipeline: The HIV prevention research pipeline has delivered more effective and acceptable prevention products, such as CAB-LA, DVR, and dual prevention pill (DPP). Research is ongoing on easier-to-use formulations, such as gels, implants, films, and inserts. Antibody formulated interventions offer hope for a vaccine product.

ii. Limited access to PrEP alternatives: Novel efficacious options are still missing from the Kenyan HIV prevention toolkit, with no clear plans for their availability. CAB-

Despite tremendous efforts to curb HIV epidemic, a significant proportion of the population remains at risk.

This research concentrates on building a body of evidence on the accessibility and availability of HIV prevention tools, as well as the potential risks that intellectual property rights pose to the availability of affordable and necessary medicines and healthcare products for HIV prevention.

LA and DVR will soon be available but only within demonstration projects, limiting access to those able to join the CATALYST study or former participants of the ViiV Healthcare sponsored study. Market entry for these novel products is dependent on intellectual property rights, with voluntary licensing for CAB-LA unlikely to result in market entry for at least 2-3 years.

iii. Market entry barriers for novel PrEP products. CAB-LA and DVR face the following market entry barriers in Kenya:
   - Intellectual property rights: Voluntary licensing for CAB-LA is unlikely to result in market entry for at least 2-3 years.
   - Regulatory approval: CAB-LA regulatory approval is yet to be secured in Kenya, despite approval by stringent regulatory authorities and recommendation by the World Health Organization (WHO).
   - Financing: PEPFAR support for CAB-LA rollout is tentatively scheduled for 2025, and PEPFAR funding cannot be used to procure DVR for country rollout, except for implementation research, without US Food and Drug Administration (US FDA) regulatory approval of DVR.
   - Delivery pathways and demand: KEMSA and government public health facilities have the required machinery to roll out injectable PrEP, but product integration into the existing pipeline, financing for cascaded systems, and appropriate service delivery mechanisms need to be considered.

iv. Concerns of condom affordability: A projected shortage in government-provided free condoms is forcing individuals to spend out-of-pocket, potentially limiting affordability. A pack of condoms trading at between KSh. 50 to 400 may be unaffordable, especially for vulnerable populations.

HIV prevention research has advanced to provide more efficacious and acceptable alternatives in the fight against HIV. Kenya needs to accelerate the incorporation of CAB-LA and DVR into the national prevention toolbox, including sustaining condom supply, to realize the potential of combined intervention. Access, affordability, and availability play a significant role in determining implementation timeline and success, and should be navigated with support from global partners and input from local stakeholders.

We therefore recommend the following actions:

i. Incorporate new HIV prevention interventions into the country's combination prevention package. Prioritize interventions proven superior to the existing standard of care, such as CAB-LA.
ii. Utilize local legal systems to exploit TRIPS flexibilities. This could allow faster market entry for generic CAB-LA products and cheaper local manufacturing. Encourage the use of voluntary licenses and parallel importation for highly effective HIV prevention options.
iii. Ensure approval of CAB-LA by the Pharmacy and Poisons Board. Use fast-tracked marketing approval channels, such as partial reliance on stringent regulatory authorities or joint-reviews with countries where review is still ongoing.
iv. Engage global partners to fast-track funding for CAB-LA and DVR. Start implementation during the demonstration projects to quickly effect lessons learned.
v. Consolidate PrEP demand across regions and countries and utilize pooled procurement. Identify countries with high PrEP uptake and utilization to build consensus and drive negotiations.
vi. Evaluate product delivery and integration pathways. Consider finances for cascaded systems and service delivery mechanisms that are sensitive to HIV prevention uptake barriers. Design product introduction and related services with the end user in mind.
vii. Subsidize the cost or declare condoms tax-free to ensure affordability.

1.0 INTRODUCTION

Globally, in 2022, there were an estimated 39 million people living with HIV (PLWH), and 1.3 million new infections annually[1]. The number of HIV infections and AIDS-related deaths have continued to decrease globally, largely attributed to improved access to treatment, however much needs to be done to reach the global target of 200,000 new infections annually by 2030[2].

Sub-Saharan Africa (SSA) is a region accounting for 50% of new infections across the globe and more than 50% of PLHW, however the biggest decline since 1980s in new HIV infections was reported in 2022[3]. The UNAIDS target of 95:95:95[2], meaning 95% of the population to know their HIV status; 95% of those testing positive to be put on treatment; and 95% of those on treatment to be virally suppressed, has been the drive by most countries towards ending the HIV epidemic by 2030. By 2022, six African countries (Botswana, Eswatini, Namibia, Rwanda, Tanzania and Zimbabwe) had achieved the targets and at least 8 other African countries (Nigeria, Burundi, Sao Tome and Principe, Kenya, Lesotho, Malawi, Seychelles and Zambia) were within reach of these targets[4]. Pre-exposure prophylaxis coverage in Africa is estimated to be about 10% of the target high-risk population, with an estimated 2.7 billion condoms distributed across the continent to fill a demand of about 6 billion condoms[4]. Countries are combining proven prevention options to bring about large reductions in new HIV infections.

Kenya ranks among the top 12 high HIV burden countries in Africa, with an HIV prevalence of 4.9% and an estimated 1.5 million PLWH[5]. The rates of new HIV infections in Kenya have steadily declined over the years, with the annual rate falling by nearly 25% between 2018 and 2020[6]. The national survey estimate that 36,000 people are infected annually (incidence rate of 0.14%) among those aged 15-84 years old[5], against an epidemic control target of 0.01%[2]. The UNAIDS 95:95:95 targets stand at 79.4% of the population know their status, 95.7% of those with a known status are on treatment, and 88.4% of people on HIV treatment have suppressed viral loads[5]. While Kenya may have a generalized HIV epidemic, higher incidence rates have been reported among key and vulnerable populations including adolescent girls and young women (AGYW), men who have sex with men (MSM), female sex workers (FSW), injection drug users (IDUs) and fisher-folk communities (FF)[7,8].

Despite the tremendous progress to curb the epidemic in Kenya, a significant proportion of the population still remains at risk of HIV infection. The Kenya demographic health survey (KDHS) of 2022[9] reported that about 50% of both men and

women have heard of pre-exposure prophylaxis (PrEP). On multiple sexual partnerships and higher-risk sexual intercourse, it found that the average number of sexual partners in a lifetime for men and women aged 15–49 is 7.4 and 2.3, respectively. Among those aged 15-49, it determined that 19% and 35% of women and men respectively had intercourse with a person who was neither their husband or lived with them in the past year, of whom 37% of females and 68% of males used a condom. On knowledge and practice about HIV prevention among young people, it reported that 60% of young women and men aged 15–34 have knowledge about HIV prevention. These remain tangible indicators for more knowledge on HIV and related risks, and driver for demand of HIV prevention interventions. The gap for HIV prevention remains significant, with global and national targets beyond reach. The need for effective combination prevention to drive towards zero new HIV infections, and curb the epidemic by 2030 target, remains a necessity.

1.1. Background

The evolution of HIV prevention interventions has been driven by advances in science and technology, as well as by a better understanding of how HIV is transmitted and how to prevent transmission. HIV prevention interventions can be classified broadly into three main categories: behavioral, biomedical, and structural interventions (see Figure 1).

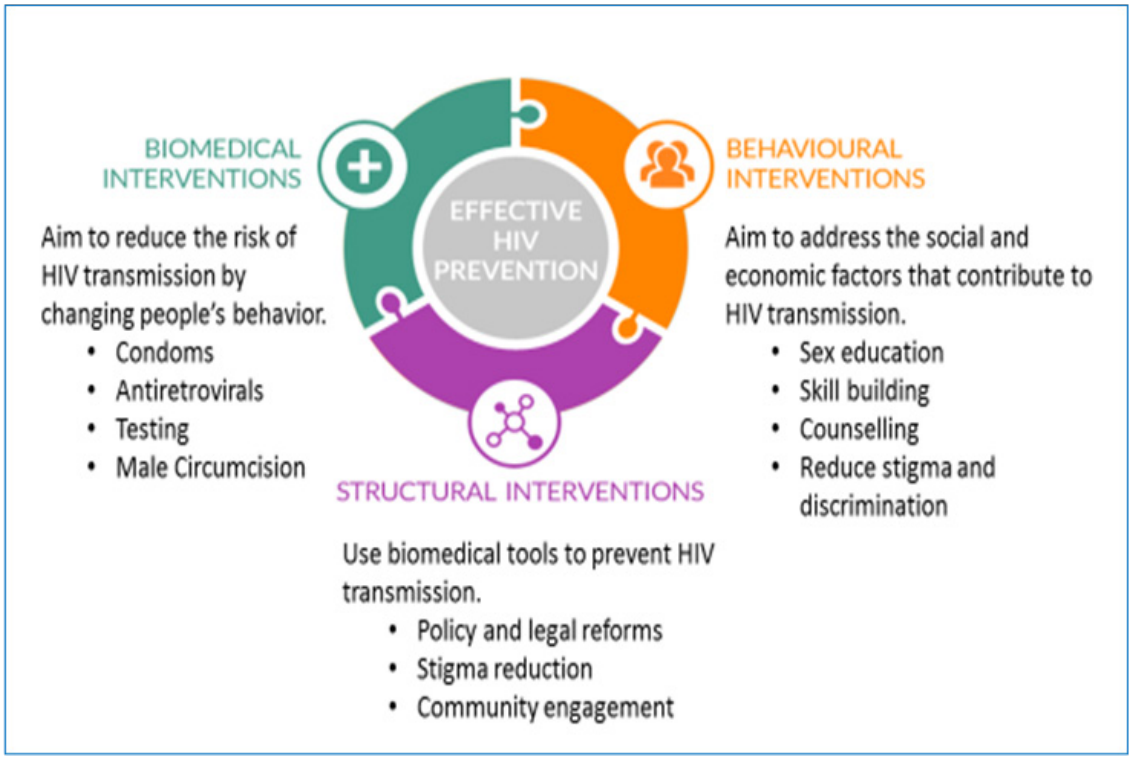


Figure 1: Categorization of HIV prevention Strategies

Since 2010, a number of major international research have demonstrated the effectiveness of using antiretrovirals (ARVs) to prevent the transmission of HIV[10,11]. These studies highlighted existing ARVs' dual potential in preventing and managing HIV transmission. Treatment as Prevention (TasP) involves using current treatments to reduce infectivity in individuals with HIV, while PrEP entails HIV-uninfected individuals using ARVs to prevent HIV acquisition. The global spotlight is on these interventions, with strong appeal for their wider accessibility in regions where those at highest HIV risk currently lack access to effective interventions[4].

Advancements in HIV prevention research have led to the creation of long-acting biological HIV prevention methods, which eliminate the need for daily pill administration and offer continuous protection against contracting HIV. Currently in Kenya, pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) require daily ingestion of antiretroviral medicines. Long-acting HIV prevention tools offer alternative, acceptable, discreet and convenient choices for highly effective HIV prevention[12]. Cabotegravir injection (CAB-LA) and dapivirine vaginal rings (DVR), even though shown to be efficacious and approved in some countries, remains inaccessible to most individuals at risk in Kenya. There is a need to conduct research to understand access and barriers to access to these novel interventions.

This research is nested under the project titled "Challenging Intellectual Property Barriers that Prevent Access to Treatment for Persons Living with HIV in Kenya." It primarily concentrates on building a body of evidence on the accessibility and availability of HIV prevention tools, as well as the potential risks that intellectual property rights pose to the availability of affordable and necessary medicines and healthcare products for HIV prevention. It also offers advocacy recommendations. A policy brief created as a result is a tool for advocacy to better inform policymakers and legislators on how to increase access to, availability of, and affordability of the HIV prevention tools, as well as to facilitate engagements with and accountability by the government.

1.2. Aims and Objectives

This report evaluates the status of HIV prevention interventions, intellectual property and legal hurdles to access, availability, and affordability in the Kenyan and regional markets. The specific objectives of the report include:

- Outline the classification of HIV prevention tools, and describe the status of availability, accessibility and affordability.
- Investigate intellectual property and legal and policy barriers to access, availability and affordability of HIV prevention tools.
- Develop a Policy Brief based on the findings.

1.3. Methodology

This research combined desk-top review of available literature to determine new HIV prevention interventions, including description of the HIV prevention biomedical pipeline. Specific focus was on PrEP modalities, available evidence, and novel interventions. Depending on gaps in reviewed literature, we reached out to key informants within the country to confirm the country's status on the interventions of interest.

1.3.1. Approach

We conducted published scientific literature search in MEDLINE, using appropriate search terms depending on outcome of interest. We did desk-top review of all relevant identified materials relating to novel HIV prevention options, their adoption and country approval status, including concerns about their accessibility, availability, and affordability. Further review was done on related scientific abstracts made in recent HIV conferences including conference on retroviruses and opportunistic infections (CROI), international conference on AIDS and STI in Africa (ICASA), HIV research for prevention (HIVR4P) and international AIDS scientific conference (IAS). Kenya specific data was obtained through review of local surveys including demographic and health survey (KDHS), AIDS indicator survey (KAIS), and population-based HIV impact assessment (KENPHIA), and government reports from various ministries including ministry of health and the national treasury and economic planning. Global partners' reports offered both regional and country specific funding and programmatic outcomes.

From online sources, we reviewed the role of local and international intellectual property regulations, including effects of World Trade Organization (WTO) agreements such as agreement on Trade-Related aspects of Intellectual Property Rights (TRIPS). We further reviewed World Health Organization (WHO) recommended HIV interventions, and approval status from leading stringent regulatory authorities including US Food and Drug Authorities (FDA) and European Medicines Agency (EMEA). Further reviews focused on sub-Saharan and Kenya specific documents and policies relating to the subject matter, including pharmacy and poisons board (KPPB) approved products.

To further understand in-country restrictions, we conducted qualitative interviews with key respondents. Interviews were based on our review of the literature mainly to fill in already identified local policy or legal gaps, and to shed light on ongoing country plans that may not be documented. The target respondents were from the Kenya Pharmacy and Poisons Board (KPPB) product registration unit, and ministry of health (MoH) - National AIDS and STI Control and Prevention (NASCOP) staff mainly leading the national HIV prevention interventions roll out. Interviews were structured depending on need.

1.3.2. Validation

[A validation workshop was conducted to get insight and fill gaps within the draft documents. Applying nominal group consensus approach, whereby before the scheduled meeting, members received the draft documents via email for their read and general comments. Feedback was received before the face-to-face or virtual meeting and were categorized and summarized. During the planned meeting, the documents were presented in summary, specific contentious issues raised as per the feedback, and discussed for any further input or consensus. All feedback were incorporated into subsequent revised versions.

2.0 CLASSIFICATION OF HIV PREVENTION TOOLS

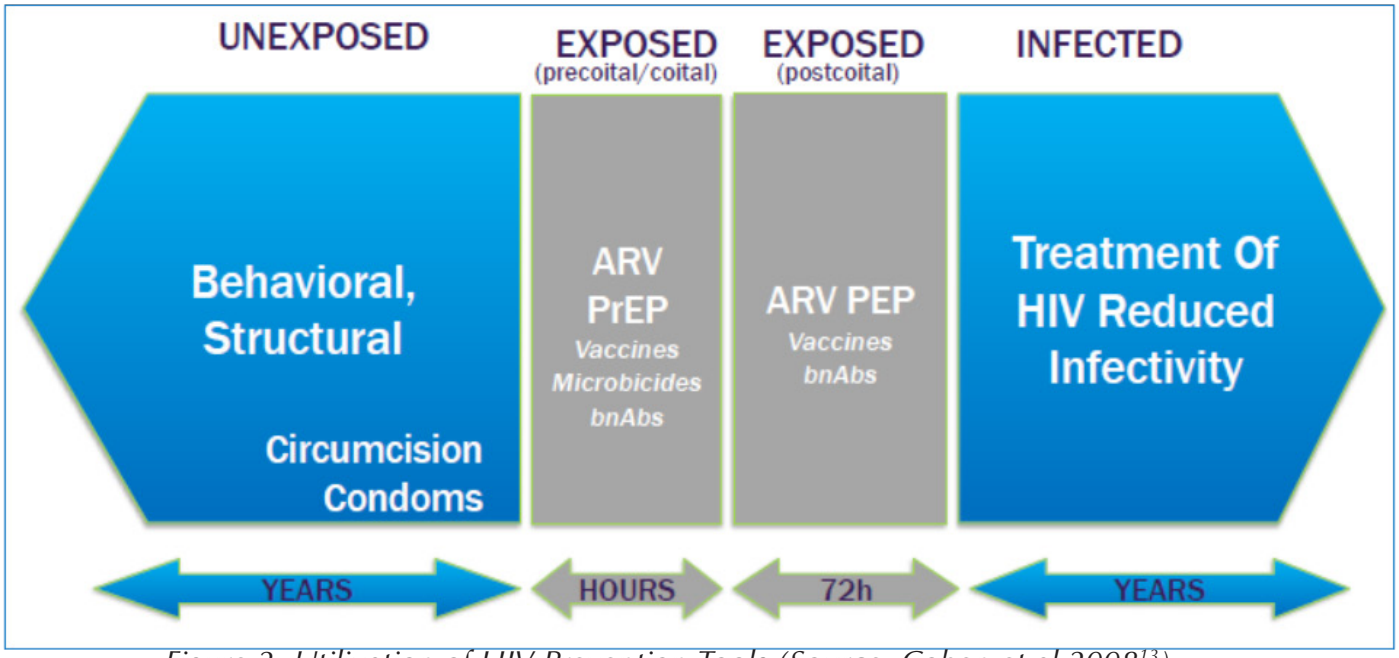


Figure 2: Utilization of HIV Prevention Tools (Source: Cohen et al 2008[13])

While different types of intervention classification exist, we will focus on utilization of the intervention relative to risk as primary means of broad classification. Within each broad classification, there are specific intervention types in that category, including those available and those undergoing clinical evaluation.

HIV prevention tools have been classified broadly by the utilization window relative to high-risk sexual encounter. The products would then be used by individuals depending on whether they are unexposed, exposed or already infected. Intervention targeting those unexposed but remain at risk due to high prevalence of HIV within their environments would be suitable to receive **condoms** or **voluntary male medical circumcision (VMMC).** Generally behavioral and structural strategies would focus on preventing HIV in this population, before actual exposure. Some interventions may be useful at the point of exposure, but before sexual intercourse, as they are effective in prevention viral entry at the time of primary infection. These interventions include potential vaccines, antiretrovirals useful **as pre-exposure prophylaxis (PrEP), and possibility of effective broadly neutralizing antibodies (bNAbs).** While soon after high-risk sexual encounter, with possible viral exposure but without infection, prevention interventions may be useful in preventing viral cell entry, hence preventing infection. Intervention useful at this point are antiretrovirals used as **post-exposure prophylaxis (PEP)** and potential **broadly neutralizing antibodies (bNAbs).** Where infection has already set in, **treatment as prevention (TasP)** may be used to reduce transmission of the virus to uninfected sexual partner, mainly by initiating antiretroviral therapy on index case and reducing the viral load to undetectable levels.

2.1. Antibody Formulated Interventions

Antibodies are part of the body's natural defense system to fight off infection and are generally produced in the course of an infection. Similarly for HIV infection, the body produces virus specific antibodies conferring protection against HIV infection[14], hence some individuals are able to suppress the HIV viral replication for a long period of time based on the characteristics of their immune response i.e. elite controllers / suppressors. From these individuals, researchers have been able to harness broadly neutralizing antibodies (bNAbs), which block a wider range of HIV strains than other antibodies by targeting areas of the virus that are slower to mutate[14]. There is an interest in passive immunization with monoclonal antibodies (mAbs) modeled on these naturally-occurring bNAbs to prevent HIV-1 infections.

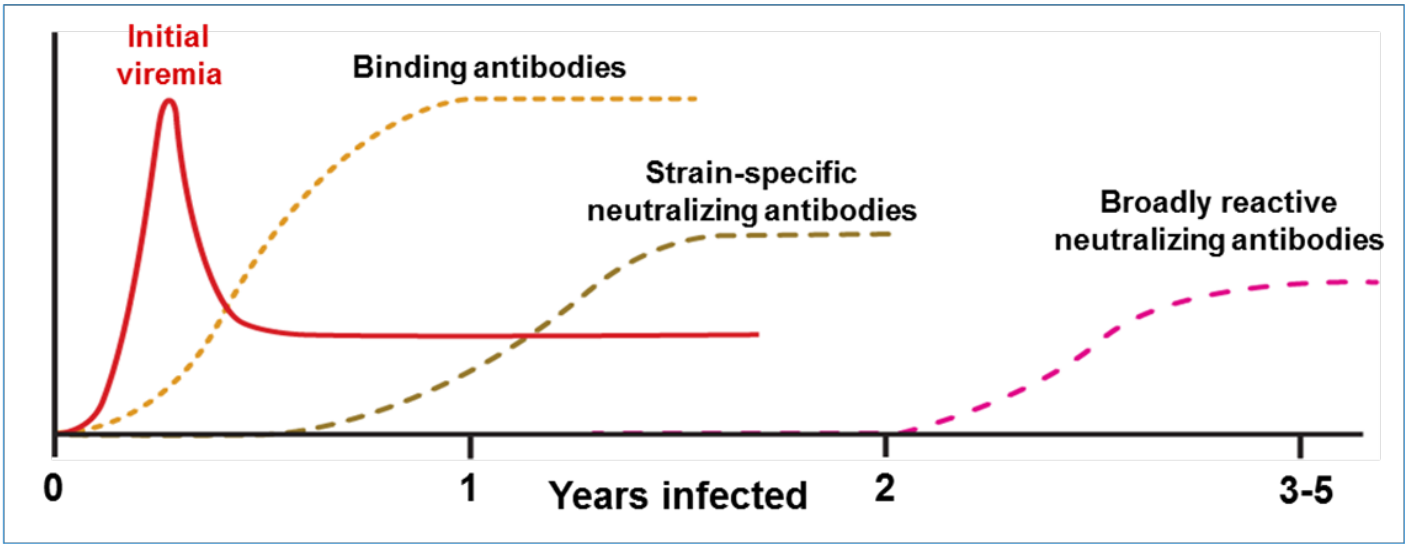


Figure 3: Development of broadly neutralizing antibodies during natural HIV infection
Source: Euler and Schuitemaker, 2012[15]

About 5-30% of PLWH naturally develop bNAbs after 2-3 years following infection[15]. While bNAbs may not necessarily suppress infection in the host individual in the long term due to continuing viral mutation, they may prevent viral replication in someone else with a susceptible strain. Given they are natural, they may have the advantage of being potentially long acting, safe and non-toxic. Different types of bNAbs have been isolated from hosts, copied and manufactured to be tested for HIV prevention, common one being VRC01. Two landmark studies evaluated VRC01 effectiveness in prevention HIV among MSM and transgender in the Americas (HVTN 704/HPTN 085), and among women in SSA (HVTN 703 / HPTN 081), with results showing VRC01 could prevent HIV-1 infection, but prevention efficacy was dependent on the sensitivity of circulating viruses to VRC01[16]. While prevention efficacy was high (75%) against viruses that were sensitive to VRC01, there was no significant protection overall. Second generation multiple bnAbs are to have better coverage and higher potency, and used in combination to improve population strain effectiveness[17,18]. They will need to be proven to be safe, highly efficacious, durable and easily administered, offering simple prevention and treatment regimens, affordable, scalable, and offer high genetic barrier for viral resistance[19].

Availability, access, and affordability: Research is ongoing to formulate bNAbs and deliver a product that will work at scale, across an entire population, to prevent HIV infection. While no products are close to approval, potential challenges related to affordability and accessibility are compounded for monoclonal antibodies that are inherently more difficult and costly to develop and produce than standard ARVs[19]. There is need to begin with the end in mind, to ensure access, manufacturing, licensing, and delivery methods are thought through way before the effective product is discovered.

2.2. Condoms

Condoms provide a physical barrier that effectively prevent the exchange of bodily fluids during sexual intercourse, offering protection against sexually transmitted infections (STIs) and unintended pregnancies. Both external and internal condoms have revolutionized sexual health and have been instrumental in empowering individuals to take charge of their reproductive choices.

i. **External Condoms:** These condoms are worn over an erect penis, creating a barrier that prevents the transmission of HIV and STIs. They have the advantage of being readily available, often low cost or free, multiple protection, and can be carried easily and discreetly. However, they have the disadvantage of potential irritation for those allergic or sensitive to latex, requires

commitment of both partners, and may lip off or break.

ii. **Internal Condoms:** Formerly known as female condoms, these are worn inside the vagina or anus. They play a pivotal role in sexual and reproductive health and rights (SRHR), providing a non-hormonal multipurpose prevention method (MPT) initiated and controlled by women or receptive sexual partners.

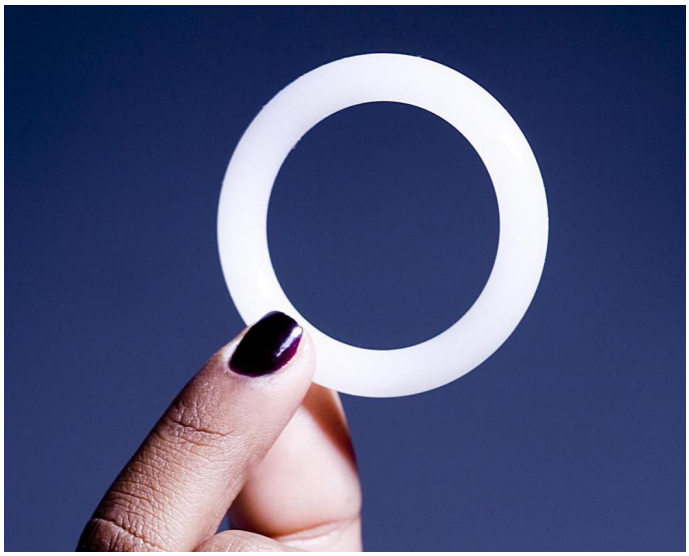
iii. **Lubricants:** Often used in conjunction with condoms, enhance comfort and reduce friction during sexual activity. They contribute to increased condom usage by improving satisfaction and encouraging consistent and correct application. Water-based lubricants are typically recommended to prevent condom damage and maintain effectiveness[20].

Both types of condoms, when used consistently and correctly, are highly effective, with a potential efficacy of up to 95% in protecting against STIs, including HIV[21]. Their significance as widely accessible and cost-effective tool in the fight against HIV/AIDS underlines their pivotal role in preventing HIV and promoting overall sexual health.

Availability, access, and affordability: Condoms are inexpensive, ranging in price from KSh. 50 to KSh. 400 for a pack of three condoms, and can be purchased from most retail outlets, street vendors, pharmacies and supermarkets. These include both locally manufactured and imported brands. Government's effort with support from donors has been to provide free condoms at government health facilities and designated public spaces, however this supply is currently capped at about 150 million condoms against an estimated 400 million in terms of annual demand[22]. There are lingering concerns on sustainability of free condoms, with imminent stockouts of the same. This apparent gap in free supply necessitates out of pocket spending to fill the gap, with a potential for unmet need among those who may not be able to purchase them. There is less than universal condom use among sexually active individuals, as country survey data indicate that while 19% and 35% of women and men respectively had sex within the last 12 months with a non-cohabiting partner, only 37% and 68% of the women and men respectively used a condom[9].

2.3. Microbicides

Microbicides are products that could be applied to or inserted into the vagina or rectum to safely prevent HIV acquisition through sexual exposure. They may be ARV or non-ARV based, with different formulations for presenting the active ingredient. They have the advantage of being user-controlled and offer discreet and easy-to-use tools to address unmet prevention needs. They work to prevent infection directly at the site of exposure (i.e. the rectum or vagina).



CAPRISSA 004 study showed that 1% vaginal gel formulation of tenofovir reduced HIV acquisition by an estimated 39% overall, and by 54% in women with high gel adherence[23]. In terms of product safety, there was no increase in the overall adverse event rates, and there were no changes in viral load differences or tenofovir resistance in HIV seroconverts. This paved the way for different formulation of antiretrovirals for easier vaginal and rectal use. Vaginal ring, containing an antiretroviral (Dapivirine), was tested in two parallel independent studies; the MTN-Aspire study which determined the ring to be 37% effective in preventing HIV acquisition

among high-risk women with disparity in age and adherence levels[24]. The Ring Study independently also showed 31% effectiveness in preventing HIV infection[25]. When evaluating preference among AGYW before user experience, similar proportions stated a preference for the ring and oral PrEP (38.1% and 40.5% respectively), with 19% of participants stating they preferred both products equally[26]. Following user experience, most participants had high adherence in 50.2% of ring and 22.4% of oral PrEP users, while acceptability varied, with 88.5% liking ring and 63.9% liking oral PrEP[27]. The Dapivirine vaginal ring has been subsequently approved for use as HIV prevention option. In early phase clinical evaluation, is a tenofovir only vaginal ring[28].

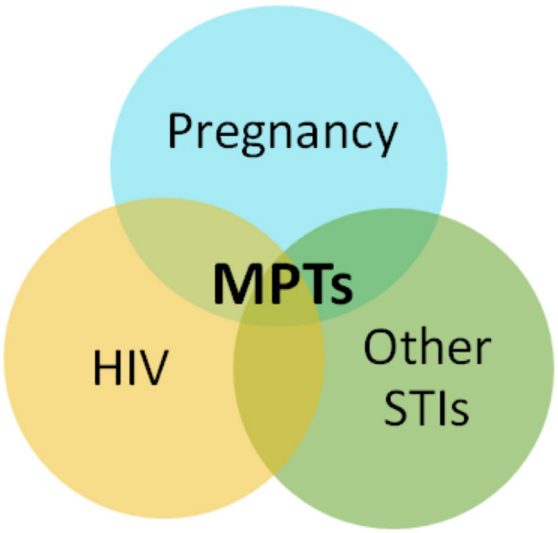
Rectal microbicides, designed to reduce the risk of HIV and other sexually transmitted infections during anal sex, are currently being studied. They can take various forms such as gels, douches, suppositories, or rectal tablets. Promising products in development, including a reduced glycerin formulation of tenofovir gel[29], Dapivirine gel[30], and rectal insert containing tenofovir and elvitegravir[31].

For some individuals, topical products that can be applied or used around the time of sex and provide protection to a part of the body exposed to HIV may be preferable to pills or injections, which provide systemic protection. Microbicides offer a "user-controlled" option, one that empowers people to protect themselves without relying on healthcare workers to insert or remove a device.

Availability, access, and affordability: Currently, the only approved product is Dapivirine vaginal ring, which was approved by European Medicines Agency (EMA) in 2020. The product got WHO recommendation in 2021. Within Kenya, the product is approved by the pharmacy and poison's board (KPPB), and included in the Kenya HIV prevention guidelines of 2022 but with a caveat that further instructions on implementation to follow, hence not directly available within the public health supply chain[32]. There is potential for availability within the CATALYST demonstration project as an alternative option for oral PrEP to trial participants. While PEPFAR does not plan to procure the ring for programmatic implementation, it will purchase for implementations science studies at a price of about USD 13 per ring[33].

2.4. Multi-Purpose Technology

Multipurpose Prevention Technologies (MPTs) encompass a spectrum of innovative products strategically designed to address various sexual and reproductive health (SRH) concerns within a single, user-friendly solution. Traditional examples such as male and female condoms, which provide protection against both pregnancy and STIs including HIV, have long been established as early instances of MPTs. A clarion call for discreet, user-controlled products capable of addressing multiple SRH needs has resonated, particularly among women, more specifically young women[34]. These needs encompass not only HIV and other STI prevention but also contraception, reflecting a broader desire for comprehensive SRH care. Advocacy for similar products extends to men who have sex with men (MSM) and transgender individuals, emphasizing the need for MPTs that can combat a range of STIs, including HIV[35].



MPTs are multifaceted in their formats, encompassing co-formulations (combinations of multiple drugs within a single product) and co-packaged products (administering two distinct

products as a pair). The MPT landscape is dynamic, with numerous products progressing through pre-clinical and clinical trials, representing a critical step towards providing individuals with a spectrum of options to meet their evolving SRH needs across their lifetime[36]. The diversity in the MPT pipeline underscores the commitment to developing personalized and holistic SRH care, empowering individuals to take proactive steps in managing their health and well-being.

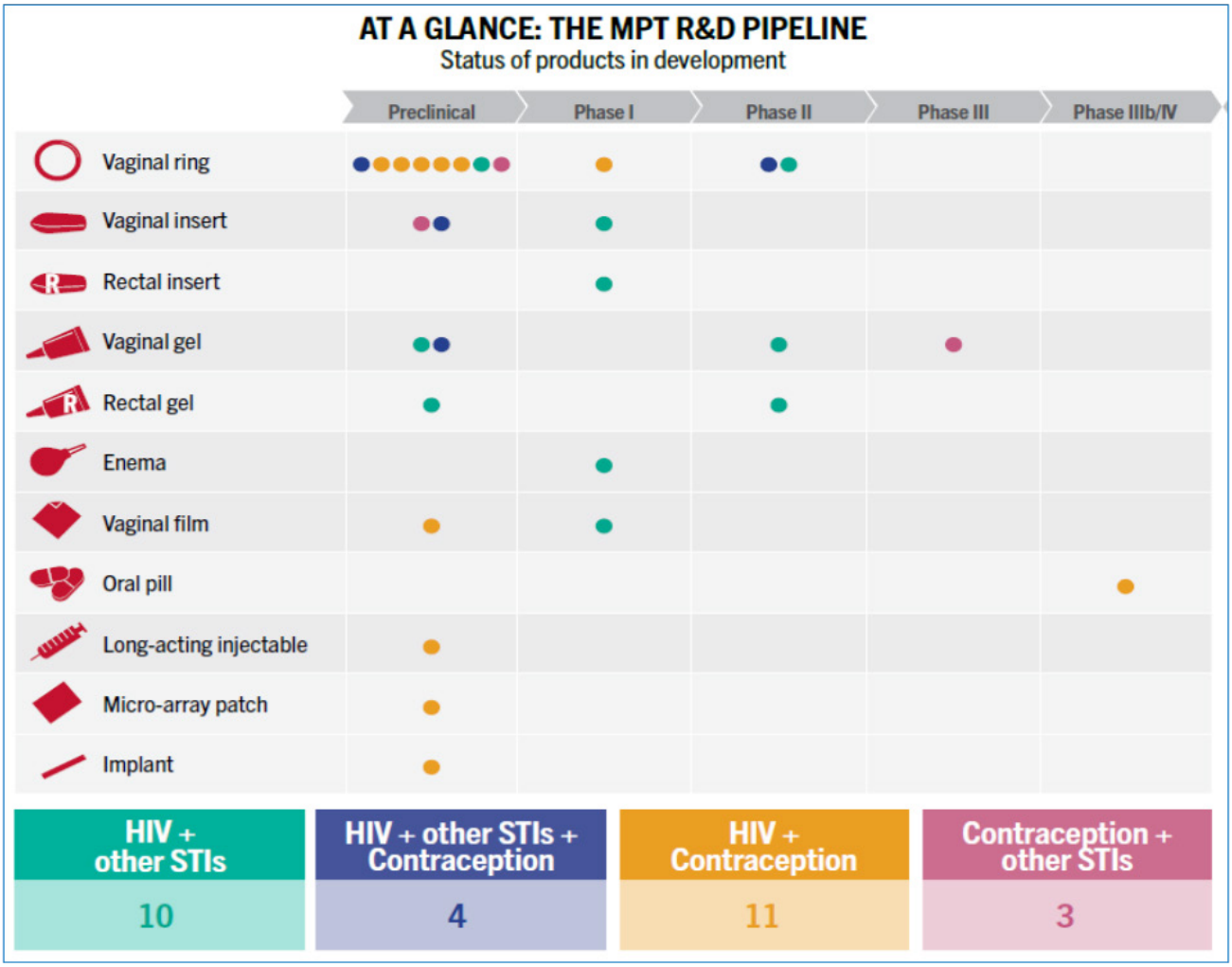


Figure 5: Multi-Purpose Technology Pipeline (Source: AVAC)

Fig 6: MPT Vaginal Ring

Key products further in the MPT development pipeline include tenofovir gel for prevention of HIV and HSV-2. Vaginal rings formulated with tenofovir for HIV and HSV-2 prevention, as well as a dual product vaginal ring containing Tenofovir and Levonorgestrel for HIV, HSV-2 and pregnancy prevention, have been initially evaluated within the country with acceptable drug delivery and positive feedback on acceptability[28,37], however more research on effectiveness are needed before the products are ready for market approval. One noteworthy MPT in the advanced stages of research is the Dual Prevention Pill (DPP), designed for HIV and pregnancy prevention in women[38]. The DPP ingeniously combines TDF/FTC-based oral PrEP with Levonogestrol / Ethinyl estradiol oral

contraceptives (OC), offering a comprehensive solution for simultaneously addressing two critical SRH concerns.

Availability, access, and affordability: While all new MPTs are largely in clinical evaluation, the DPP is the closest to registration and roll out given it combines two already approved and proven efficacious products. Based on a planned evaluation starting in 2023, application for registration may be submitted in 2024, with potential for public roll out in 2025[39].

2.5. Post-Exposure Prophylaxis

Post-Exposure Prophylaxis (PEP), sometimes referred to as PEPSE (Post-Exposure Prophylaxis following Sexual Exposure), represents a pivotal intervention in the realm of HIV prevention, offering an intervention in situations of known or suspected HIV exposure. This strategy involves a brief course of antiretroviral medications administered promptly after the potential exposure, with the primary objective of mitigating the risk of HIV infection. Time is of the essence in PEP administration, as its efficacy diminishes with delays in initiation[40], hence to maximize its effectiveness, PEP must commence within a tight window of 72 hours following the potential HIV exposure. The regimen entails daily medication for a duration of 28 days, a proactive measure aimed at thwarting the virus's ability to establish a foothold within the body[41]. PEP may involve various antiretroviral regimens, providing flexibility in its application. In Kenya, recommended regimen include combinations of tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and dolutegravir (DTG) for those ≥ 15 years, with the option of replacing TDF with abacavir (ABC) for those < 15 years and <30 kgs[32]. Future developments in PEP may introduce novel drug combinations or improved formulations, potentially optimizing efficacy and adherence. The availability of PEP underscores the commitment to comprehensive HIV prevention, ensuring that individuals have access to immediate interventions when confronted with potential HIV exposure.

Availability, access, and affordability: PEP medication is generally available across all health facilities providing HIV care and management across the country. It is provided free of charge in public health facilities. The Kenya guidelines require initiation within 72 hours of exposure, mandatory HIV test before initiation with eligibility assessed based on type of exposure, HIV status of source where possible and timing of seeking care[32].

2.6. Pre-Exposure Prophylaxis

Pre-Exposure Prophylaxis (PrEP) is medicine (usually ARVs) taken to prevent HIV, offering a pre-emptive shield against the virus. ARVs, originally developed to treat people living with HIV, have emerged as potent agents to prevent HIV acquisition among HIV-negative individuals[42].

Approved PrEP options include:

i. **Oral PrEP:** - When used consistently and correctly, oral PrEP significantly reduces the risk of HIV infection, and has been shown to be effective in different population segments including MSM[43] and heterosexual couples[42], with further varying evidence due to adherence concerns[44]. The first oral daily PrEP pill gained FDA approval in 2012, and contained tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) [FTC/TDF]. More recently, tenofovir alafenamide (TAF) and emtricitabine [F/TAF] was approved by FDA in 2019, with a better safety profile mainly in terms of renal glomerular function biomarkers and bone mineral density[45]. However, F/TAF received approval initially for MSM and transgender women, with ongoing efficacy studies examining its effectiveness among cisgender women[46].

ii. **Injectable PrEP:** In a significant development, Cabotegravir (CAB-LA) gained first global regulatory approval in 2021 as the first injectable PrEP option. A study comparing CAB-LA to TDF/FTC showed that both products were generally

safe, well tolerated, and effective, however CAB-LA was superior to FTC/TDF in preventing HIV infection among high-risk cis-gender men and trans-gender women who have sex with men[47] and in individuals assigned female at birth[48]. The injectable is given every 8 weeks, as intramuscular injection to the gluteus muscle. A newer long-acting product undergoing clinical trial (Purpose Study) is Lenacapavir[46], which is injected sub-cutaneously twice a year, with clinical trials expected to conclude in 2025.

iii. **Vaginal Ring:** The dapivirine vaginal ring received a positive opinion from the European Medicines Agency in 2020, with WHO approval for HIV prevention in 2021. This discreet and user-controlled product offers another effective option for HIV prevention, particularly for individuals who may prefer alternative forms of PrEP[24]. Details are provided under microbicides and multi-purpose technology above.

The field of PrEP research and development continues to diversify with an array of innovative products in various stages of development. Early-phase development includes patches, gels, douches, implants, films, vaginal and rectal inserts, topical agents, as well as formulations of long-acting and short-acting products fast-tracked though USAID-funded MATRIX (A Project to Advance the Research and Development of Innovative HIV Prevention Products for Women)[49]. Further along in development are a three-monthly ring, a multipurpose technology combining PrEP with contraception, and longer-acting injectable formulations[50]. These advancements reflect a commitment to comprehensive HIV prevention, ensuring that individuals have a range of options tailored to their unique needs, hence offering choice.

Availability, access, and affordability: Introduced in 2017, oral PrEP medication is generally available across all health facilities providing HIV care and management across the country. It is provided free of charge in public health facilities. The Kenya guidelines require initiation of PrEP following HIV risk assessment and confirmation of HIV negative status[39]. Currently, approximately 360,000 individuals have been initiated on PrEP in Kenya, however national survey indicate that 48% and 49% of women and men respectively have knowledge of HIV medications to treat or prevent HIV infection[5]. Challenges exist with integration of PrEP services into facilities and community programs, which is likely to address concerns regarding low uptake, inadequate differentiated services, high discontinuation rates, and knowledge gaps, healthcare worker attitude and service quality concerns[51]. While included in the national guidelines, CAB-LA and dapivirine rings are marked as undergoing approval and availability, hence further implementation guidelines will be made available on their use within public health facilities. CAB-LA is estimated to cost between $35-45 at manufacture[52], and will require PEPFAR purchasing support in which Kenya is marked as the next batch of countries to be considered[51]. Meanwhile, CAB-LA will remain available within demonstration projects which aim to evaluate implementation of an enhanced service delivery package providing informed choice on PrEP products mainly among women. These projects include MOSAIC - CATALYST study supported by USAID and PEPFAR[53], and extended access research protocol for HPTN 084 study participants supported by ViiV healthcare.

2.7. Treatment as Prevention

Antiretroviral treatment has not only revolutionized the care of people living with HIV but has also emerged as a powerful strategy in the prevention of HIV transmission. The profound impact of ARV therapy on reducing HIV viral load and preserving the health of individuals was demonstrated in a study that showed ART was associated with a 93% lower risk of linked partner infection, with no linked infections observed from among stably suppressed individuals[10]. Decades of scientific evidence have demonstrated that ARV medications reduce the quantity of HIV in an individual's body, effectively suppressing the virus[54]. With

diligent adherence to treatment, viral levels can plummet to a point where standard diagnostic tests no longer detect the virus (undetectable). One of the most significant breakthroughs in HIV prevention and destigmatization is encapsulated in the phrase "Undetectable = Untransmittable" (U=U). This simple yet transformative message underscores a critical fact: when an individual living with HIV consistently adheres to ART and achieves an undetectable viral load, they cannot transmit HIV to their sexual partners[55]. Recent evidence has shown that there is almost zero risk of sexual transmission of HIV with viral loads of less than 1000 copies per mL[11].

Availability, access, and affordability: ARV medications are generally available across all public health facilities providing HIV care and management across the country. It is provided free of charge in public health facilities. The Kenya guidelines require initiation of antiretroviral therapy for anyone who tests positive for HIV infection. Of the estimated 1.4 million Kenyans living with HIV, about 96% of those who know their status are on treatment, of whom 90.6% of them have achieved viral load suppression[5].

2.8. Vaccines

Vaccines ability to confer immunity against infectious diseases has reshaped the course of human health[56], setting the stage for the pursuit of an HIV vaccine. The urgency for a safe, effective, and accessible HIV vaccine cannot be overstated as such a vaccine holds the promise to bring about a durable end to the HIV pandemic. However, the path to an effective HIV vaccine is fraught with complexity, given the virus's intricate and ever-evolving nature.

Thai RV144 vaccine demonstrated that the prime-boost vaccine regimen was safe and modestly effective in preventing HIV infection, lowering the rate of HIV infection by 31.2%, hence the only HIV vaccine to show efficacy[57]. Even though the vaccine combination was based on HIV strains that commonly circulate in Thailand, RV144 and its follow-on research allowed researchers to discover correlates of risk, provided targets for optimizing vaccine boosting, and provides a critical comparison for more recent HIV vaccine candidate trials[58]. Modification of the vaccine target site, using more potent diluent and better boosting strategy for effectiveness in clade C virus mainly circulating in Southern Africa, led to the Uhambo Trial (HVTN 702), which stopped early in 2020 because data showed the vaccine did not prevent HIV acquisition, however was safe[59]. Modification of the vaccine to increase vaccine coverage, led to development to quadrivalent vaccine, candidate for Imbokodo trial (HVTN 705), which was also stopped in 2021 as the vaccine regimen was safe but did not provide sufficient protection against HIV for the women enrolled in the study[60]. Further modification to target clade B predominant in Europe and the Americas developed a candidate vaccine for Mosaico Study (HVTN 706), which in 2023 announced that the vaccine regimen was safe but was not effective in preventing HIV infection among MSM and transgender people[61]. Further data analysis in these trials will help inform future research.

One notable endeavor in the realm of HIV vaccine research is the ongoing phase IIb trial known as the PrEPVacc trial[62]. This trial introduces a novel approach by combining experimental vaccines with oral pre-exposure prophylaxis (PrEP). While both vaccine candidates have not been successful in late-stage trials on their own, PrEPVacc is testing to see if they are more effective when used with PrEP. The outcome of this trial could potentially validate a T-cell vaccine strategy, marking a significant milestone in the field. The study results are expected in 2024.

In the broader landscape of HIV vaccine research, recalibration and adaptation are underway. The field is diligently analyzing the outcomes of major trials that explored strategies ultimately deemed ineffective[63], and research is focusing on two key parts of the immune system: broadly neutralizing antibodies and T cells, with new approaches, including mRNA vaccine platforms, providing promise in the future[64].

Availability, access, and affordability: Currently no HIV vaccine is close to getting

out of the research pipeline. The pursuit for vaccines may require utilization of novel technology, however they should be easy and not costly to manufacture rapidly in order to address equity and have an impact across the globe.

2.9. Voluntary Male Medical Circumcision (VMMC)

Voluntary Medical Male Circumcision (VMMC) has proven effective in reducing HIV transmission by approximately 60%[65], and since the procedure cannot be reversed, this partial protection continues throughout a man's lifetime. The procedure is simple and completed either through a quick surgical procedure by a trained health professional, or a non-surgical device-based method administered by a healthcare provider. Other circumcision devices which aim to make the procedure easier, quicker and more widely accessible include:

- **PrePex Device:** A device which works by compressing the foreskin between a ring and an elastic band, leading to distal tissue necrosis (death). This device was approved by WHO in August 2016, following findings from studies conducted in Rwanda, Zimbabwe and Kenya[66]. This novel device employs a controlled radial elastic mechanism, rendering the procedure quicker and virtually painless, thus attracting more individuals to opt for circumcision.

Fig 7: PrePex Device

- **ShangRing:** It consists of two concentric rings that sandwich the foreskin of the penis, allowing circumcision without stitches or notable bleeding[67]. In addition, it provides substantially reduced operative times, low complication rates, and a technique that can easily be taught to non-physician personnel.

Fig 8: ShangRing

As VMMC continues to evolve, ongoing research and innovation ensure that it remains a formidable tool in the fight against HIV, progressively adapting to the needs and preferences of communities.

Availability, access, and affordability: About 94% of men aged 15-49 years are either traditionally or medically circumcised in Kenya, of whom 57% are medically circumcised[5]. VMMC is available free of charge, supported by PEPFAR with specific focus on five traditionally non-circumcising counties (Migori, Kisumu, Homa Bay, Siaya and Turkana) and two culturally circumcising counties housing large populations of migrant non-circumcision groups (Nairobi and Nandi)[51]. The remaining counties are deemed to be traditionally circumcising and have male circumcision rates > 80%.

2.10. Combination Prevention

Combination prevention is a set of strategically-selected interventions that are rights-based, evidence-informed, employing a mix of biomedical, behavioral and structural interventions, prioritized to meet the HIV prevention needs of individuals

and communities, and is delivered at the scale needed to make an impact on reducing HIV infections. There has been a growing focus on combination prevention approaches that use multiple interventions together to achieve the greatest impact, most of the interventions mentioned above in addition to targeting population segments and employing both behavioral and structural interventions. The five pillars of combination HIV prevention are AGYW, key populations, condoms, VMMC and PrEP. The national rollout of HIV program ensures combination prevention messages and implementation customized to the needs of the local community and population segment.

2.11. The Future of HIV Prevention Arena

The HIV prevention arena is dynamically evolving, propelled by groundbreaking research and innovation. A multiplicity of interventions, each with its unique strengths, are paving the way towards a future where HIV transmission is markedly reduced, if not eradicated. The future of HIV prevention lies in the convergence of innovative biomedical solutions, personalized strategies, holistic approaches, community empowerment, and accessible policies. Currently, the HIV prevention toolbox has the following biomedical interventions which have been shown to be effective and safe in humans, with approval from at least one regulatory authority across the globe.

Table I: Approved Biomedical HIV Prevention Toolbox

Intervention	Description	Earliest Evidence
Condoms	• Internal	1980 [68]
	• External	1920 (Latex condoms) [69]
Oral PrEP	• Tenofovir Alafenamate (TAF) / Emticitabine [F/TAF]	2020 [45]
	• Tenofovir Disoproxil Fumarate / Emtricitabine [FTC/TDF]	2010 [43]
Injectable PrEP	• Cabotegravir Long-Acting (CAB-LA)	2021 [47,48]
Microbicides	• Dapivirine Vaginal Ring (DVR)	2016 [24,25]
Voluntary Male Medical Circumcision (VMMC)	• Procedure based	2008 [65]
	• Device based	2013 [66]
Antiretroviral	• Used as PEP	1995 [42]
	• Used for treatment (TasP)	2016 [10]

The projected time to market for novel HIV prevention interventions is shown below, relative to recently approved alternatives.

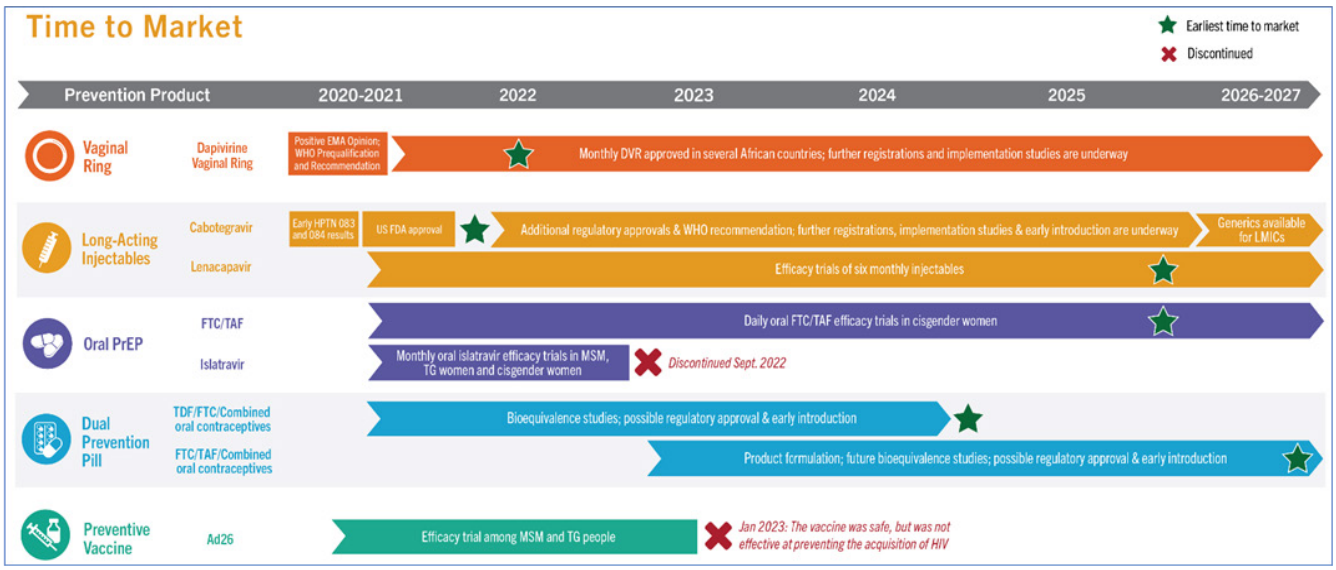


Figure 9: HIV Prevention Products Pipeline (Source: AVAC)

3.0 INTELLECTUAL PROPERTY, LEGAL AND POLICY BARRIERS

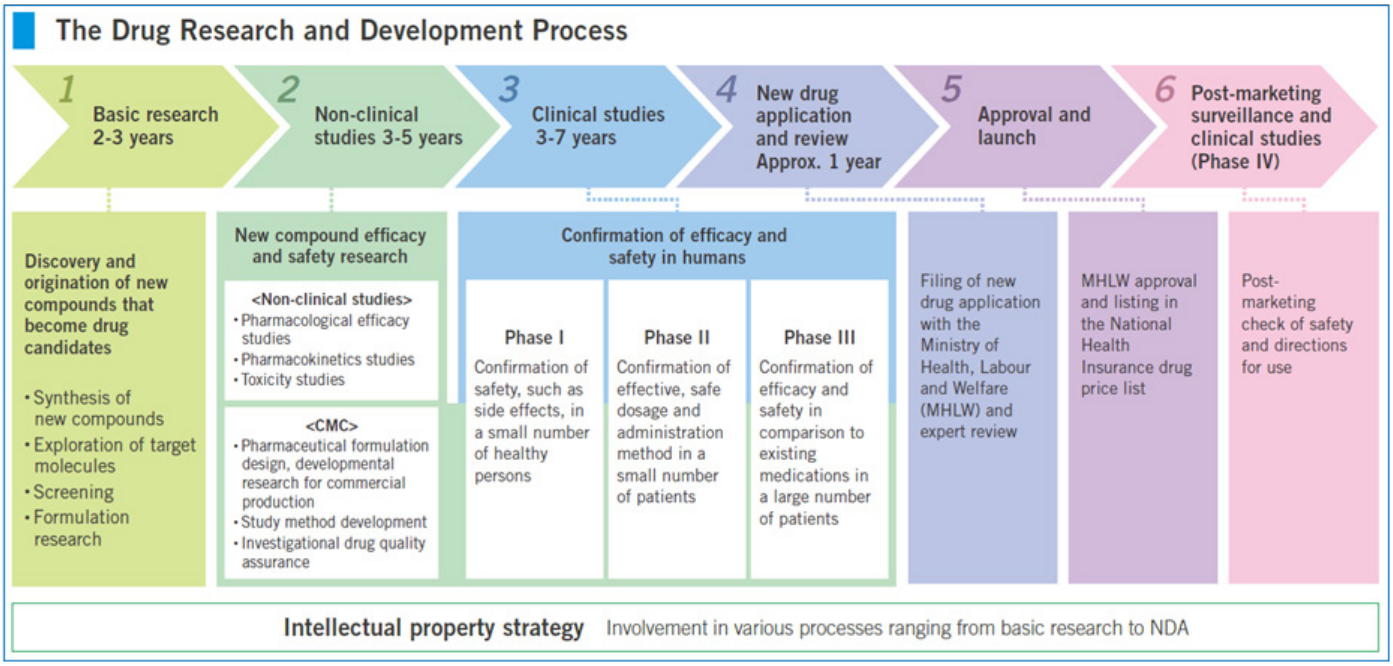


Figure 10: Process of New Drug Development (Source: Seikagaku Corporation)

3.1.The Drug Development Process

The drug development process **(Figure 10)** is complex and time-consuming, taking around 25 years before market release[70]. Only a few compounds make it to market after rigorous clinical evaluation.

This process comprises four phases: discovery, pre-clinical research, clinical research, and market approval[71]. Discovery involves identifying potential molecular compounds, either from new technology or repurposed products, often protected by intellectual property rights[72]. Pre-clinical research assesses toxicity and distribution in non-human animals over four to seven years. Clinical research tests compounds in humans, ensuring ethical and scientific safeguards[73]. It includes multiple phases, from safety and dosing (Phase I) to efficacy and safety (Phase III). Marketing approval applications are submitted based on data up to Phase III, targeting stringent regulatory authorities[74].

We review drug development and introduction challenges related to novel ARVs like long-acting cabotegravir (CAB-LA), Dapivirine vaginal ring (DVR), and Emtricitabine/Tenofovir alafenamide (F/TAF) for PrEP.

3.2. Intellectual Property Rights

Intellectual property rights (IPR) grant legal protection to inventors or creators, allowing them to safeguard their creations for a specific duration and derive recognition and financial benefits[75]. In the pharmaceutical sector, IPR serves as an incentive for research and development, assuring innovators that their products will be safeguarded from competition for a limited time upon market entry[76].

However, this system becomes more complex for products intended for populations with a small potential market or urgent needs, particularly during epidemics and pandemics. Low and middle-income countries, comprising over 80% of the global population, account for only 10% of global drug sales due to affordability and accessibility challenges[77].

Intellectual property rights (IPR) encompass various forms, with each playing a distinct role in biopharmaceutical development:

1. Patents: These are awarded for an innovation satisfying the criteria of global novelty, non-obviousness, and industrial or commercial application, and can be granted for a product or processes[78]. Patents grant exclusive rights for

20 years, preventing the production of generic products and delaying market entry of biosimilar generics[79] that impact public health, as seen with HIV.

Potential barriers could stem from the following:

- Data exclusivity, also known as data protection, limits the use of innovator's clinical data for generic drug approval, hindering access to cheaper alternatives.
- Market exclusivity prevents third parties from obtaining regulatory approval for a specific pharmaceutical product for a set period, encouraging R&D investment[80].
- Secondary patenting extends patent life by covering aspects beyond the active ingredient[81], a process termed evergreening. This limits market entry of generic drugs.
- Patent term extension prolongs protection beyond 20 years due to delays in marketing approval or classification as an orphan drug.
- Patent linkage connects generic drug approval to the patent status of the branded equivalent[82], prohibiting entry of generic drugs before expiry of a patent or without the consent of the patent owner.

Kenya operates within a multi-layered IP regulation framework, including the Kenya Industrial Properties Institute (KIPI), signatory status with the African Regional Intellectual Property Organization (ARIPO), and membership in the World Trade Organization (WTO); entailing adherence to the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)[83]. These agreements streamline inventor protection across member countries.

Global intellectual property protection impacts access to medicines, affecting pricing, local generic production, imports from off-patent countries, and generic market entry delays[84]. TRIPS, a core WTO agreement, sets minimum IP standards for pharmaceutical products, offering flexibility measures like compulsory licensing, Bolar provision, limited patent scope, definitions of invention, parallel importation, and the least developed country (LDC) transition period[85,86]. A definition of these flexibilities is detailed in **Appendix I.**

The 2001 WTO Doha Declaration reaffirms states' rights to employ TRIPS flexibilities to enhance health and medicine access[87]. An analysis of TRIPS database in Africa showed that these flexibilities, particularly compulsory licensing, LDC transition periods, and parallel importation, were mainly used for HIV/AIDS treatments[88]. Kenya previously pursued parallel importation and compulsory licensing for HIV medication, leading to voluntary licensing by GSK and Boehringer Ingelheim to a local manufacturer, Cosmos Ltd[89].

To improve access to novel ARVs, Kenya could legislate for broader flexibilities, such as stringent patentability criteria, limited patent term extensions, and data protection limitations, facilitating quicker market entry of generic medicines. Enforcement challenges for compulsory licensing include limited local generic production capacity[90]. Parallel importation poses a risk of counterfeit products entering the market[91].

Product Development Partnerships (PDPs) use research expertise, global networks, and resources to reduce the risk of commercial investment; often requiring that products be affordable and broadly accessible[92]. PDPs like the International Partnership for Microbicides (IPM) have launched novel HIV prevention products, such as the Dapivirine vaginal ring. Licensing strategies, like those of the Medicines Patent Pool (MPP), expand access to underserved markets. Founded by UNITAID in 2010, MPP secures voluntary licenses from pharmaceutical firms, sublicensing access-friendly terms for HIV products[93]. In July 2022, ViiV healthcare issued a voluntary license to MPP for cabotegravir injection for PrEP, leading to sub-licenses for Aurobindo, Cipla, and Mylan, mainly covering high HIV burden areas, including sub-Saharan Africa[94]. Gilead, the manufacturer of F/TAF, has previously shown willingness to enter voluntary agreements with manufacturers in developing countries to serve less developed markets for their FTC/TDF PrEP formulation.

3.3. Regulatory and Guidance

Clinical evidence for medicine safety and efficacy is submitted to national regulatory authorities for market approval. Some economic blocks rely on regional regulatory authorities like the African Medicine Agency (AMA) aim for harmonized reviews[95]. First submissions often go to WHO stringent regulatory authorities (SRA) with a plan for accelerated local approvals within non-SRA drug authorities[96]. Currently, no African country has an SRA, necessitating national regulatory authority (NRA) submissions even after external approval. Diverse requirements and regulations hinder concurrent submissions across multiple countries, extending approval timelines[97].

Medicines procured through agreements or donor support require WHO prequalification98. This ensures quality, safety, and efficacy while supporting NRA capacity-building. Fast-tracking prequalification is crucial to expedite access for those in need. Challenges include reliance on prior SRA assessments, prompting calls for reliance-based approval networks[97].

The 25-year gap from clinical trial to marketing approval[70] is lengthy for an effective HIV prevention product. Authorization for emergency use authorization and reliance on regional review bodies, like in the case of COVID-19 vaccines, can significantly reduce approval timelines. Kenya can leverage initiatives to reduce review timelines and redundant submissions. Slow access to novel interventions in low and lower-middle-income countries (LIC/LMIC) is due to varying regulatory requirements, lack of mutual recognition, and lengthy reviews[99]. Collaborative registration procedures like WHO Accelerated Registration of Finished Pharmaceutical Products approved by SRAs, EU-medicines for all (EU-M4all), Swissmedic's marketing authorization for goal health products (MAGHP), and EAC medicines regulatory harmonization facilitate NRA approvals and capacity-building[100,101,102,103]. Despite progress, underutilization, poor NRA recognition, and limited scope hinder their impact[99]. KPPB needs to swiftly deploy existing pathways and create new strategies for faster regulatory approvals, embracing mutual recognition and collaborative registration for HIV prevention products. KPPB's recent guidelines on emergency and compassionate use authorization[104], may affect the eligibility of novel ARVs.

CAB-LA was FDA-approved in December 2021, WHO-recommended in July 2022, and is approved in nine countries with submissions in 15 more as of October 20, 2023[105]. Kenya's Pharmacy and Poison Board received the submission in December 2022, awaiting local approval. The Dapivirine vaginal ring, approved by the European Medicines Agency in 2020 and recommended by WHO in 2021, is approved by the Kenya Pharmacy and Poisons Board [REF?]. Speedy regulatory approvals, including WHO prequalification for countries without in-country approvals, are vital to ensure public access to these products.

3.4. Financing

To streamline product consideration, national drug lists and HIV prevention guidelines should include them before purchase[106,107]. As guidelines and lists are periodically revised, supplementary or tentative inclusion should accommodate future HIV prevention products approved elsewhere but not locally yet. This ensures timely inclusion in recommendation documents to prevent implementation delays.

The Kenya HIV Prevention and Treatment Guidelines of 2022 include CAB-LA and DVR with dosing instructions but note their varying stages of approval and availability in Kenya[32]. Specific implementation guidelines will follow. The guidelines further provide for use of TAF in those with renal impairment and need TDF and establishes that TAF may become preferred once available in fixed-dose combination. However, the 2019-updated Kenya Essential Medicines List lacks details on novel antiretrovirals like CAB-LA, DVR, and TAF. Integration into WHO policy guidance is pivotal for broad adoption, as it aligns products with leading funders and procurers[108]. Evidence on benefits, harms, community preferences, adherence, cost, feasibility, equity, and resistance impact informs policy and guideline updates for new HIV prevention products[107].Proactive dialogue and evidence gathering are essential for eventual policy inclusion.

Early donor engagement is crucial for product integration into funding strategies. Large funders like PEPFAR and the Global Fund have collectively invested over $126 billion in the global AIDS response[109,110], with Kenya allocating KSh. 24.8B (about USD 165M) in the 2023/24 national budget for HIV, TB, and Malaria programs as a contribution to the Global Fund[111]. PEPFAR allocated $347M in the same year, contributing to a total of about $777.4M for HIV response[51].

As PEPFAR support transitions[112], Kenya plans a shift from donor to government support for key health programs in the 2023-2027 medium-term plan[113]. With ongoing Global Fund support, countries must prioritize interventions within their allocated funds in alignment with WHO recommendations[110]. Stakeholders, including technical partners and civil society organizations (CSOs), will play a crucial role in grant planning and prioritizing new products to address funding gaps and ensure the inclusion of innovative prevention technologies in national strategies.

Ensuring affordability for novel HIV prevention products alongside generic and biosimilar competition requires new strategies. Product Development Partnerships (PDPs), like the International Partnership for Microbicides, support affordability and accessibility. Initiatives such as MATRIX[49] and the MOSAIC (Maximizing Options to Advance Informed Choice for HIV Prevention) consortium work to expedite research and development and enhance product introduction, access, and scale-up[53]. Local partners in Kenya, like LVCT Health and FHI 360, collaborate with the Ministry of Health to advance access and uptake of various HIV prevention products in a multiproduct market, including oral PrEP, CAB-LA, and DVR.

3.5. Procurement

Affordability is crucial in procurement, and financing mechanisms should involve global partners to lower manufacturer prices through large-scale programs or cost reduction. Kenya collaborates with Global Fund and PEPFAR to secure support for costly HIV prevention options. PEPFAR included Kenya in the waiting list for CAB-LA allocation in the next cycle starting in 2025, subject to change. For DVR, PEPFAR requires FDA approval for funding procurement, but supports implementation from other sources[33].

Innovative public-private collaborations, including PDPs, voluntary licensing, and mechanisms like advanced market commitments (AMC), volume guarantees, and buy-downs, stabilize pricing dynamics for affordable access.

Table II: Negotiations strategies to support affordability of medicines.

Negotiation Strategy	Description
Advanced Market Commitments (AMCs).	Guarantors provide a financial commitment to subsidize the future purchase of health commodities at negotiated prices based on anticipated public health impact and expressed demand, hence the company can invest in large-scale production.
Volume guarantees	Explicit agreements by buyers to purchase a minimum quantity of an existing product, typically matched with a long-term supply contract that sets pricing thresholds. It allows buyers to negotiate lower prices and better terms, which can stimulate demand and uptake.
Buy-downs	Time-limited subsidies to reduce pricing and catalyze uptake for new technologies that are deemed of critical public health value, but for which initial market dynamics pose a challenge to affordable pricing. They help to foster broad global uptake until more sustainable, volume-based price reductions can be achieved.

Global Fund and PEPFAR cover approximately 80% of ARV procurement in LIC and LMIC[110], with SSA accounting for 70% of global ARV demand[114]. Pooled procurement platforms play a vital role in aggregating volume and leveraging pricing negotiations, ensuring affordability for HIV prevention products[115]. As countries transition from donor support to financial independence[116], early transition discussions and pooling demand with similar-interest partners are essential to maintain large-volume purchase benefits and long-term delinking from donor funding streams. This will avoid price variations and ensuring access to existing and new products.

3.6. Product Delivery

The product introduction framework comprises five stages, from planning to monitoring, offering unique considerations for effective rollout of novel HIV prevention products to reach the target population. Long-acting HIV prevention technologies can significantly impact the epidemic if implementation barriers are overcome, demand is generated, and optimal delivery models are defined.

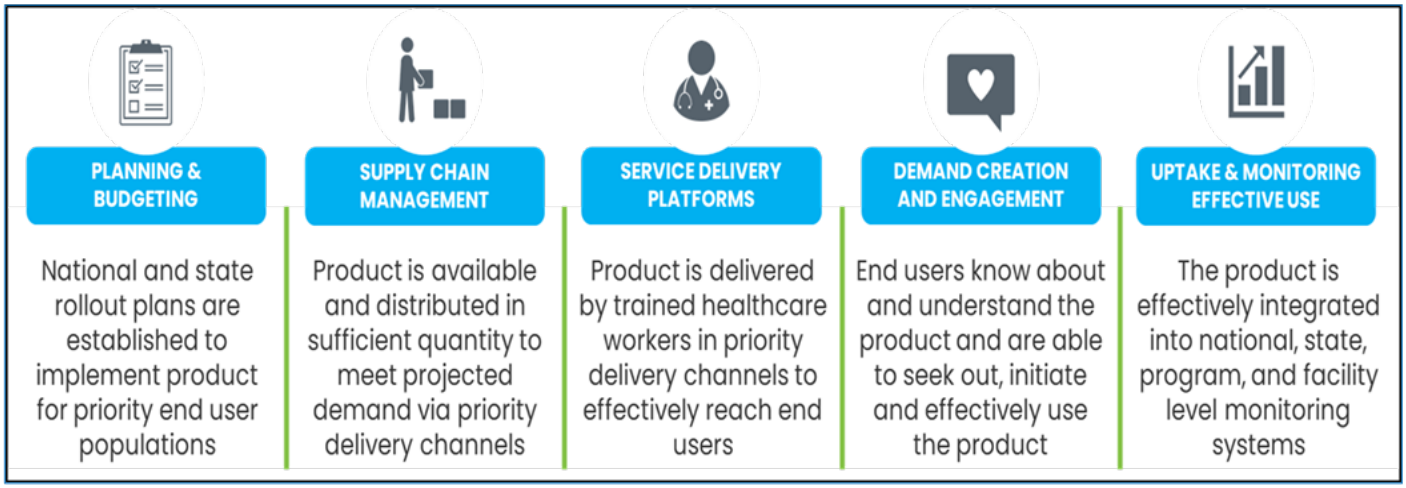


Figure 11: The Product Introduction Framework (Value Chain)

Challenges in implementing long-acting HIV prevention products may include stigma, product attributes, limited demand, socio-cultural barriers, and delivery obstacles[117]. Early engagement is essential to design messaging and delivery with end-users' needs and preferences in mind.

Planning and budgeting: Effective national introduction necessitates situation analysis, opportunity assessments, policy guidance, financing, and procurement. Key steps include creating national introduction plans, prioritization through scenario analysis, health provider guidance, integration into logistic and health information systems, and robust communication and community engagement[118]. Adequate financing down to subnational levels must also be ensured.

Supply chain management: Countries should conduct supply chain assessments to identify deficiencies and infrastructure needs, considering shifts in demand from existing products. Kenya already has a supply chain system through Kenya Medical Supplies Agency (KEMSA) supported by implementation partners, with depots across the country for health facility and patient support center supply.

Service delivery platforms: Effective delivery should be convenient, affordable, and integrated into health system access points for at-risk populations. Differentiated service delivery strategies that adapt to diverse needs[119] and move beyond traditional sites, such as community-based services or mobile outreach, can enhance uptake and adherence[120].

Demand creation and engagement: Certain population segments, particularly vulnerable groups like adolescent girls and young women (AGYW), face challenges accessing HIV services, contributing to new HIV infections[121]. Additionally, healthcare providers are often not equipped to address the needs of these key populations[122].

AGYW face high infection risk due to societal factors like poverty, discrimination, and gender-based violence[123]. Women generally are often unable to compel their HIV-negative partners to participate in prevention measures[124]. Legal barriers and adult-oriented services also discourage young people[125]. Key populations, including men who have sex with men (MSM), people who inject drugs (PWID), and sex workers (SWs), often remain marginalized in health service delivery systems.

4.0 RECOMMENDATIONS AND CONCLUSION

Investigating intellectual property, legal, and policy barriers to ARVs, including novel HIV prevention agents not yet available in the public system, this report finds and recommends:

1. Incorporation of efficacious HIV prevention options

Kenya has access to most approved HIV prevention options, largely offered for free at public health facilities through PEPFAR and the Global Fund. However, a projected shortage in government-provided free condoms is concerning, as it may limit affordability. The government should consider subsidizing condoms or offering them duty-free if donor funding is unavailable.

While Kenya's HIV prevention toolkit is nearly complete, novel efficacious options are still missing, with no clear plans for their availability. Cabotegravir long-acting (CAB-LA) and the Dapivirine vaginal ring (DVR) as PrEP options will soon be available only within demonstration projects targeting women in designated counties. This limits access to those able to join the CATALYST study or former participants of the ViiV-sponsored HPTN 084 study. CAB-LA is already proven to be superior to the current standard of care (oral PrEP), and the government should move quickly to make it available to achieve a significant impact on HIV prevention in the future. The DVR offers a choice for women and girls who may not find oral PrEP acceptable, and it may benefit them as a woman-controlled and discrete HIV prevention method while CAB-LA is still unavailable.

2. Maximizing on TRIPS flexibilities

The TRIPS agreement allows countries to institute national laws that take advantage of TRIPS flexibilities to address medicine access based on their specific context. ViiV Healthcare, the manufacturers of CAB-LA, have already allowed sub-licensing to global generic manufacturers, but access to these generics is unlikely to be possible within the next three years. During this period, Kenya should prepare for the easy introduction of generics when they become available.

While Kenya has previously utilized compulsory licensing and parallel importation, there is an opportunity to utilize the Bolar provision and limits on test data protection to allow generic manufacturers to prepare for market entry in advance. Local manufacturers have previously been allowed to manufacture ARVs through voluntary licenses, and such companies should be allowed to utilize research exemptions to determine cheaper ways to manufacture generic locally, especially for the novel ARVs that promise a larger impact when rolled out at scale.

3. Improving efficiency of the national regulatory processes.

The Kenya Pharmacy and Poisons Board (KPPB), with the national mandate to review and approve medicines, needs to consider the potential population impact of the medicine and institute appropriate measures to facilitate public access. DVR has been approved in Kenya with

support from the International Partnership for Microbicides, but the CAB-LA submission is still under review months after submission. Regulatory approval for CAB-LA has been secured in stringent regulatory authorities such as the US FDA and in nine other countries across the globe, with WHO recommendation.

There is an opportunity to activate partial reliance on stringent regulatory authorities, request joint-reviews with countries in which the review is still ongoing, or initiate information sharing with stringent regulatory authorities or WHO as they have already approved the product to fast-track the local review. While the Ministry of Health has already considered the evidence and mentioned CAB-LA and DVR in its latest guidelines of 2022, the drugs are yet to be incorporated in the essential medicines list last revised in 2019.

4. Involving global partners.

Kenya has a good relationship with global HIV partners, including the Global Fund and PEPFAR. While PEPFAR has instituted measures to ensure sustainability and transition to local government, they remain committed to supporting effective intervention rollout. Kenya is tentatively included in the waiting list of countries to receive CAB-LA support from 2025, but this is too long for a product superior to the standard of care. Through Global Fund support, Kenya could negotiate initial supply of CAB-LA to target a smaller segment of high-risk individuals to start the rollout. Given PEPFAR's position not to procure DVR until approved by the US FDA, Kenya should engage other partners to make the product available.

Other countries in sub-Saharan Africa are facing the same challenges as Kenya with the novel ARVs. Kenya should consider bilateral and multilateral discussions on suitable solutions across the region and move as a block to address access.

5. Pooling procurement and demand

Global Fund and PEPFAR pooled procurement platforms can consolidate demand, improve negotiation for better prices, and benefit from economies of scale. Even without utilizing these platforms, countries can work together to negotiate down prices using advance market commitments and volume guarantees. This will require country health ministries to coordinate efforts and consolidate demand. Identifying countries with high PrEP uptake and utilization, such as South Africa, Nigeria, Uganda, and Zambia, may help to build consensus rapidly with adequate demand to drive negotiations.

6. Reviewing internal product delivery pathways

The Kenya Medical Supplies Agency (KEMSA) and government public health facilities have established the required machinery to effectively roll out injectable PrEP, given their long-standing track record in providing care to people living with HIV and supporting immunization programs. However, there is a need to evaluate product integration into the existing pipeline and health information systems, provide financing for cascaded systems, and consider appropriate service delivery mechanisms. Healthcare workers will need to be trained and sensitized on the new commodities, including injection practices and safety measures, as service delivery has an impact on acceptability and access.

7. Creating and sustaining demand for interventions

In-country demand forecasting may include measures to increase the population utilizing PrEP and transition of all individuals using oral PrEP to CAB-LA. Specific measures, informed by discussions with users and local stakeholders, are needed to mitigate the effect of poor adherence and uptake, addressing areas such as side effects, general product knowledge, stigma, socio-economic factors, and factors of daily life. Product introduction and related services should be designed with the end user in mind, obtaining their input and addressing their concerns to ensure utilization and sustained demand. Consideration for differentiated service delivery, including community-based provision, pharmacy-based access, and mobile outreach services, would be useful to ensure high uptake and adherence specifically for those who face challenges accessing routine service points.

Conclusion

Recent advances in HIV prevention research have yielded more efficacious and acceptable alternatives to existing interventions. To realize the full potential of these new tools, Kenya must accelerate the incorporation of CAB-LA and DVR into the national prevention toolbox, while also sustaining condom supply. Access, affordability, and availability will play a critical role in determining the timeline and success of implementation. Kenya should therefore navigate these challenges with the support of global partners and input from local stakeholders for sustainable financing mechanisms.

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APPENDIX I: DEFINITION OF TRIPS FLEXIBILITIES

TRIPS flexibilities provide policy space for countries to implement the TRIPS agreement in a manner appropriate and responsive to their contexts, as different options which consider national interests and can be transposed into their national law.

Term	Description
Compulsory Licensing	Allows for the exploitation of patented subject matter through government authorization without the patent holder's consent, for reason of national emergency and public noncommercial use.
Bolar Provision	A "Bolar/early working" provision allows generic drug manufacturers to use the patented invention to obtain marketing approval without the patent owner's permission so that the generic product is approved to enter the market as soon as the patent expires.
Parallel Importation	Makes provision for importation and resale in a country without consent of the patent holder of a patented medicine put on the market of the exporting country by the patent holder or in a legal manner.
LCD Transition Period	The LDC transition period frees LDCs from TRIPS obligations related to patents on pharmaceuticals until 2033 or until they are no longer a LDC. This allows LDCs to purchase and/or produce cheaper generic medicines.
limits to the scope of patentability	Limits to second uses of known or already patented pharmaceutical products, discouraging frivolous patent and ever-greening.
definitions of invention	An interpretation of Article 27.1 of the TRIPS Agreement in national legislation in a manner that excludes new uses, formulations, dosages or combinations of previously patented medicines from patentability criteria. This legislative measure coupled with the implementation of substantive patent examination procedures would serve to prevent frivolous patent applications, ever-greening and creation of patent thickets around one invention.
Research Exemption	Allowing limited exceptions to exclusive rights conferred by patents for purposes of scientific experimentation (research exception). The research exception makes it possible for countries to develop their local scientific and technological capacities and competencies to reverse engineer pharmaceutical products for generic production and for developing them further to better suit local conditions.
Patent term extension	Countries may consider disallowing/limiting patent term extension in national law for pharmaceutical products.
Limits on test data protection	TRIPS Agreement allows countries to determine how to protect test data in the public interest. This provision demands protection from unfair commercial use and does not demand data exclusivity. Countries may therefore incorporate in domestic legislation the right of regulatory authorities to rely on available data to assess new drugs for market entry.
Creation of patent opposition (pre and post patent grant)	Required by Article 62.4 of the TRIPS Agreement, to serve as an additional administrative layer of patents review to prevent the grant of invalid patents.

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