Dual Prevention Pill

Market Preparation and Introduction Strategy

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AVAC
Global Health Advocacy, Access & Equity

CLINTON
HEALTH ACCESS
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I. Introduction

To accelerate the introduction of and access to the Dual Prevention Pill (DPP), a daily oral pill for HIV and pregnancy prevention, AVAC, Clinton Health Access Initiative (CHAI) and Mann Global Health, with support from the Children's Investment Fund Foundation (CIFF), have developed a Market Preparation and Introduction Strategy for the DPP. These organizations are part of a larger coalition – known as the DPP Consortium – working to bring the DPP to market.[1]

This strategy is intended for donors, governments, implementing partners and civil society to inform priorities and planning for DPP rollout. To this end, the strategy describes activities required to build a cohesive body of evidence and recommends an approach to introduce the DPP, enabling a focused effort. Activities are not intended to confer funding from any one donor. Where possible, activities will be embedded into existing programs to consolidate and leverage resources.

To develop the strategy, AVAC, CHAI and Mann Global Health:

Scoped and analyzed existing knowledge and evidence gaps along the research-to-rollout framework.

Sequenced, thematically organized and described activities required to build a cohesive body of evidence to support scaling of the DPP.

Validated assumptions and approach with key stakeholders, including policy makers, donors, implementing partners and civil society.

Will iterate as new evidence and information become available to respond to a dynamic prevention landscape and as activities outlined in the strategy are completed.

The original strategy was published in August 2021. This updated strategy reflects new developments through August 2023.

About the DPP Consortium

The DPP Consortium is coalition of organizations, including AVAC, CHAI, Mann Global Health, Viatris, the Population Council and Medicines360, that are implementing market preparation and introduction activities for the DPP. These efforts are supported by CIFF, the Bill & Melinda Gates Foundation (BMGF), the U.S. Agency for International Development (USAID), Catalyst Global and the HIV Prevention Trials Network (HPTN).

II. The Product and the User

The DPP would be the first product since male and female condoms to provide women with a single option for HIV prevention and family planning (FP). It offers a critical opportunity to assess whether uptake and effective use of biomedical HIV prevention increases with a multi-purpose prevention technology (MPT).

1. The product

a. Composition and packaging of the DPP

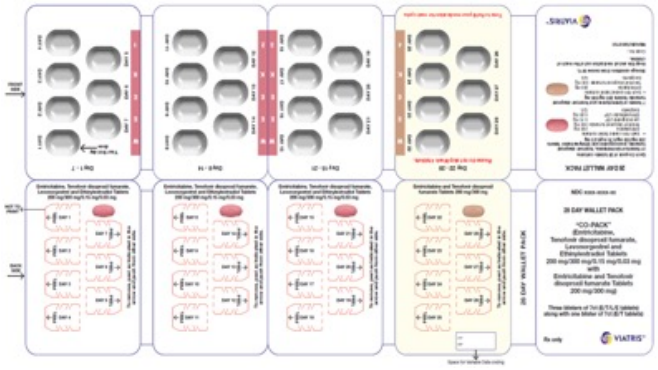
The DPP is a daily oral pill for HIV and pregnancy prevention with a 28-day regimen:

- **Days 1-21:** Tenofovir/emtricitabine (TDF/FTC, or oral PrEP) + levonorgestrel and ethinyl estradiol (LNG/EE, or combined oral contraception (COC))[ii]
- **Days 22-28:** TDF/FTC only (these pills will not contain COC to allow for monthly bleeding, as some COC packs do)

TDF/FTC is the only antiretroviral (ARV) indicated for the prevention of HIV in cisgender women and LNG/EE is the most popular COC in low- and middle-income countries (LMICs).

Figure 1: Proposed Viatris DPP tablet colors

Figure 2: Illustrative mock-up of DPP packaging by Viatris



The DPP will initially be developed and manufactured by Viatris (formerly Mylan), a generic manufacturer of oral contraceptives (OCs) and ARVs. This first-generation DPP will be a co-formulated, bi-layer tablet with differentiated colors for the first 21 vs. last 7 days. Pills will be dark pink and light peach, respectively, which were preferred among seven color options by end users in human-centered design (HCD) research conducted in South Africa and Zimbabwe.[2]

The co-formulated DPP developed by Viatris will be packaged in a cold-form blister in an accordion-style wallet pack, with instructions for use printed on the pack to guide correct use and mitigate user error. Each week will include a perforation, allowing end users to tear off sheets weekly. Branding will adopt a women's lifestyle feel and be developed in consultation with end users and civil society advocates.

Current regulatory timelines suggest the DPP developed by Viatris could receive **US Food & Drug Administration (FDA) approval in 2024**. The DPP Consortium will assess opportunities to bring other suppliers to market to encourage competition so as to increase affordability and supply security.

In addition, Population Council and Medicines360 are developing a co-formulated DPP containing LNG/EE and tenofovir alafenamide/embitricitabine (F/TAF). A second-generation DPP with F/TAF could be approximately 1/3 the size of the TDF-based DPP, and thus has potential to expand the market for women who find the tablet with TDF/FTC too large. However, F/TAF is not currently approved for cisgender women, and a clinical trial to evaluate safety and efficacy of F/TAF in women is ongoing.[3] As such, the earliest anticipated introduction of a TAF-based DPP is currently 2027.

i The term "women" is used throughout the strategy to describe the initial focus population for the DPP. Additional research or consultation is needed to determine if the DPP is safe and effective for transgender men and non-binary individuals to use.

ii Throughout the strategy, the term "oral PrEP" refers specifically to TDF/FTC (brand name Truvada) and daily oral pill-taking, while the term "PrEP" refers to all delivery methods for pre-exposure prophylaxis, inclusive of injectable cabotegravir for PrEP and the dapivirine vaginal ring. The term "COC" refers to the hormonal oral contraceptive formulation that the DPP contains (LNG/EE), whereas "OC" refers to oral contraception more generally, e.g., to describe preferences or behaviors around pill-taking that may be generalizable across OC products.

Population Council also developed an over-encapsulated DPP (a capsule containing separate TDF/FTC and LNG/EE tablets within it) for use in acceptability studies. While this product is solely for research purposes and not intended for commercial use, it will generate learnings on DPP delivery and user preferences that will further inform future research and introduction plans.

b. How does the DPP respond to end-user preferences?

End-user research studies have shown evidence of a desire for MPTs that prevent HIV and pregnancy. Discreet choice experiments suggest a higher demand for MPTs among women interested in HIV prevention compared to single-indication products.[4] For instance, the Tablets, Ring, Injections as Options (TRIO) study, conducted with women ages 18-30 in Kenya and South Africa, found participants "overwhelmingly" preferred a combined product for HIV and pregnancy prevention compared to two separate products, and that most were willing to forego their preferred single-indication product (injection) for a less-preferred product form that offered dual protection.[5] In the CUPID study, 91% of heterosexual couples in Uganda and Zimbabwe preferred MPTs over separate HIV prevention and FP products, and male partners were found to strongly contribute to women's decisions on product preferences.[6] This literature establishes a case for the development of MPTs to respond to end users' stated preferences.

c. What does the DPP offer?

As a woman-centered and controlled option that prevents HIV and pregnancy, the DPP has the potential to reach more women with oral PrEP, improve effective use and, by extension, contribute to decreased HIV incidence and unintended pregnancies. The DPP is uniquely positioned to bridge HIV and FP siloes in funding, research, health systems and service delivery. Lessons from the process of introducing and scaling the DPP, and related health systems adaptations – most notably, HIV/SRH service integration – would benefit and may accelerate rollout of future longer-acting MPTs, such as vaginal rings, injectables and implants.[7]

The DPP is likely to be introduced into a dynamic HIV prevention landscape, on the heels of the dapivirine vaginal ring (PrEP ring) and injectable cabotegravir for PrEP (CAB for PrEP). However, the PrEP ring and injectable CAB for PrEP do not provide contraceptive benefits, a concern typically more top-of-mind for women than HIV prevention.[8] The DPP should be offered to women as one option among other FP and HIV prevention products, and could be an attractive method for women who prefer the flexibility of short-acting contraceptives that are immediately reversible and user-controlled, and for whom daily pill-taking is not a barrier.

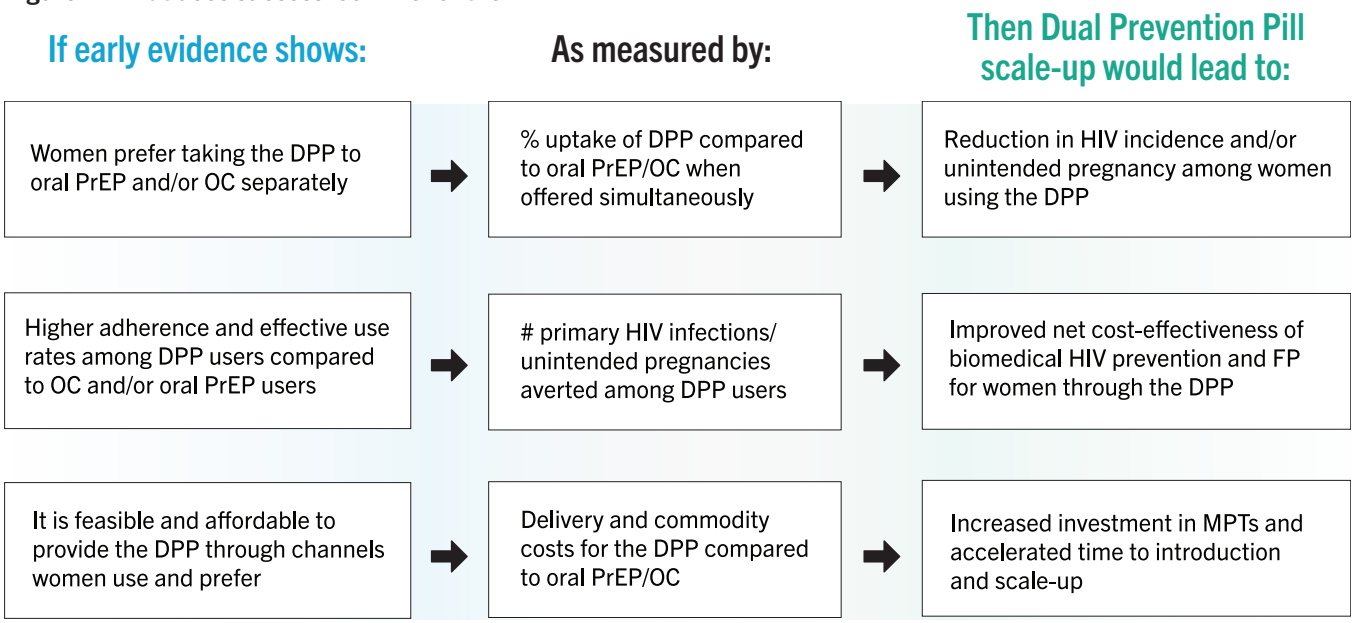
Figure 3: Potential benefits and risks associated with the DPP, by audience

Stakeholder	Potential Benefits	Potential Risks and Mitigation Plans
End Users	**Combined use can lead to better health outcomes.** A single co-formulated pill affords convenience – with protection from unintended pregnancy motivating women to adhere and continue use, including during periods of lower perceived HIV risk.[9] **A woman-controlled MPT.** The DPP provides women greater agency to mediate use. Women can mask the DPP as contraception to avoid the negative perceptions associated with oral PrEP. **Brings PrEP closer to women and builds on a shift toward self-care.** While FP is available in a variety of settings, PrEP is primarily offered in HIV clinics. The DPP may provide an impetus to re-evaluate ARV training requirements to better support integrated delivery with FP and other sexual health services, including via more decentralized delivery channels. It may also simplify access, requiring one clinic visit instead of multiple visits for separate products.	**Insufficient uptake and effective use, given that both OC and oral PrEP have high rates of early discontinuation and oral PrEP awareness is low in many settings.** Extensive end-user research will be conducted prior to introduction and draw on lessons learned from OC and oral PrEP to understand how to best engage users and support women to initiate the DPP and sustain use. Shifts to simplified, self-care approaches to oral PrEP delivery are being piloted and scaled. These better align with OC delivery and could bolster uptake and adherence to the DPP. Implementation research in real-world settings will test and evaluate delivery approaches, including how HIV testing factors into service provision and how rapid HIV and pregnancy testing can be done in parallel.

Figure 3: Potential benefits and risks associated with the DPP, by audience

Stakeholder	Potential Benefits	Potential Risks and Mitigation Plans
Providers	**Streamlines delivery of HIV and FP.** Long term, the DPP has the potential to reduce the burden on providers by delivering integrated services within a product, but this will rely on a move toward rational distribution of providers, HIV/SRH service integration and capacitation of FP providers, pharmacists and other cadres to offer HIV prevention and, in the interim, information on the DPP and where to access it. **Enables providers to respond to women's needs.** By expanding options and addressing multiple health needs, the DPP may increase women's satisfaction – a motivating factor for providers.	**Providers may be reluctant to offer the DPP** because it feels like an added burden or due to stigmatizing beliefs such as the perception it could encourage younger women to have sex and/or multiple partners. Providers will need to learn to counsel on a novel product. A working group of HIV and SRH clinical and programmatic experts developed recommendations for provider counseling messages, to be tested in DPP acceptability studies.[10] Robust civil society engagement will build literacy on the DPP in communities in advance of rollout, providing additional touchpoints for education outside of clinics.
Policy makers/ government	**Lays the groundwork for MPT introduction and evidence generation.** The DPP can bypass a large clinical trial because it combines two approved products, offering a near-term opportunity to test hypotheses on the potential improved coverage and hence population-level impact of an MPT. Future MPTs are likely to build on the regulatory, delivery and financing lessons generated from DPP introduction and scale-up. **Competitive with oral PrEP/COC separately.** If DPP use increases over time, the DPP may be lower cost than oral PrEP and COC purchased individually depending on manufacturer pricing.	**Difficulty bridging historically siloed HIV and FP programs to deliver an MPT, including separate budgets and supply chains.** Strengthening HIV/FP linkages and platforms for the DPP ahead of approval will ready health systems for other MPTs and potentially also benefit the introduction of the PrEP ring and CAB for PrEP. Adding a product with HIV prevention to both the current HIV prevention and contraceptive method mix will require greater, more intentional coordination. Growing commitment, momentum and mechanisms for integrating HIV prevention and SRH services can improve coordination across departments to facilitate DPP introduction. **With a single manufacturer for the DPP initially, supply security and affordability may be an initial concern of governments, and could deter procurement in favor of separate oral PrEP/COC.** Market shaping should be explored to expand the number of manufacturers in line with demand and to improve the value for money in commodity procurement. It will be critical to ensure these efforts do not deter procurement of oral PrEP and sensitization may be required to ensure oral PrEP remains an option for those who prefer a different product than the DPP.
Global health community	**Supports realization of an integrated approach to HIV/FP delivery, aligning donors and policy makers.** With calls for integrated solutions and an expanding HIV prevention product landscape, the DPP could attract funders interested in HIV and SRH innovations. Investing in the DPP will signal to governments, procurement agencies and implementers that MPTs are a priority.	**Constrained funding envelope with reduced resources available for FP and HIV prevention and concurrent rollouts of CAB for PrEP and the PrEP ring may limit investment.** Leveraging funding opportunities for implementation research to offer multiple products will streamline investments and potentially save costs. Reassuring the FP community and women that promoting the DPP will not jeopardize progress on long-acting methods and that the added cost of ARVs will not erect novel access barriers will be essential.

Figure 4: What does success look like for the DPP?



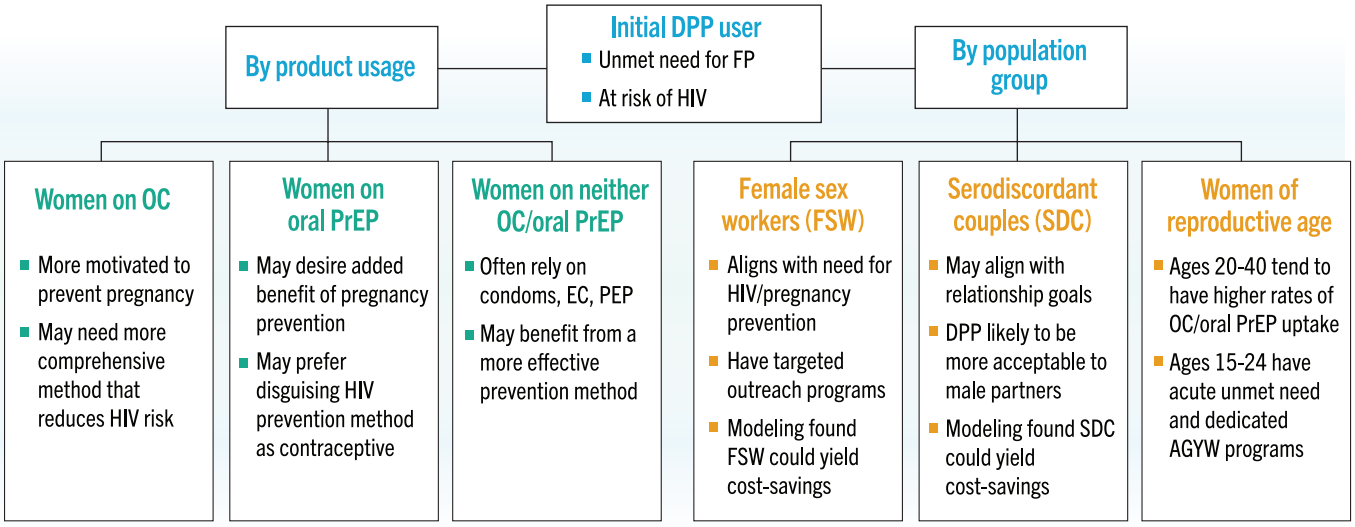
2. The user

a. DPP Focus Populations

Pending regulatory approval, the DPP will likely be indicated for all women of reproductive age (ages 15-49). However, women ages 20-40 tend to have higher rates of OC/oral PrEP uptake and effective use of oral PrEP[11] and could be early adopters of the DPP, while adolescent girls and young women (AGYW) have an acute unmet need for both HIV prevention and FP and may be interested in an MPT that addresses both.[12, 13]

Ultimately, country governments will decide on priority populations for introduction based on multiple considerations, including the current contraceptive landscape and populations at high risk for HIV, among others. DPP acceptability studies will include women ages 16-40 to understand preferences and use patterns across age groups.[14, 15] These studies and other end-user research will help to inform introduction approaches and messaging for different user segments.

Figure 5: Initial DPP focus populations



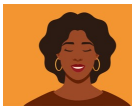
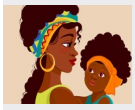
Governments could consider prioritizing particular groups of women based on country context, epidemiological trends and existing programs, which are more likely to require tailored outreach strategies. Based on this, some groups that could benefit most from DPP include:

- **Female sex workers (FSW)**: DPP cost-effectiveness modeling found that targeted delivery to FSW could yield cost-savings.[16] The DPP aligns with FSW need for HIV and pregnancy prevention, and could be integrated at targeted delivery points through existing funding (e.g., Global Fund's catalytic funding for key populations programs[17]) and peer-led and FSW outreach programs.
- **Serodiscordant couples (SDC)**: Like FSW, DPP cost-effectiveness modeling found that targeted delivery to SDC could lead to cost-savings and would have the greatest impact compared to other groups (FSW, AGYW, women ages 25-49).[18] SDC account for approximately 30% of new HIV infections in sub-Saharan Africa (SSA)[19] and may also have a desire to limit or space births. HCD research on the DPP found that end users were receptive to demand generation messaging focused on SDC.
- **Postpartum women**: Postpartum women in SSA are likely to have another child within 2-3 years[20] and may be drawn to a method with a shorter return to fertility. While COC (and thus the DPP) is not advised until 6 months postpartum, postpartum visits are an entry point for FP counseling. In Kenya, for example, PrEP is being integrated in maternal and child health (MCH) facilities, indicating that MCH providers will be trained in the provision of PrEP and SRH services and thus likely to be prepared to integrate the DPP.[21] Further, the DPP may be appealing to women given high HIV incidence in this period.[22]
- **Adolescent girls**: While they have particularly high HIV risk and incidence,[23] lessons from oral PrEP roll-out and OC use suggest lower uptake.[24] To improve uptake amongst adolescent girls, it is essential to leverage existing AGYW-specific initiatives (e.g., PEPFAR's DREAMS program,[25] the Government of South Africa's She Conquers campaign[26] and the Global Fund's HER initiative[27]), as well as adolescent-friendly services.

b. Understanding Potential DPP Users

HCD research conducted with end users in Kenya, South Africa and Zimbabwe revealed five potential initial DPP personas/archetypes based on "trigger moments" for initiating oral PrEP or COC as a proxy for the DPP.[28] These triggers, known as category entry points, hone in on potential DPP users more precisely, as they focus on end users' values, motivators and lifestyles, compared to segmenting users by broader categories such as demographics.

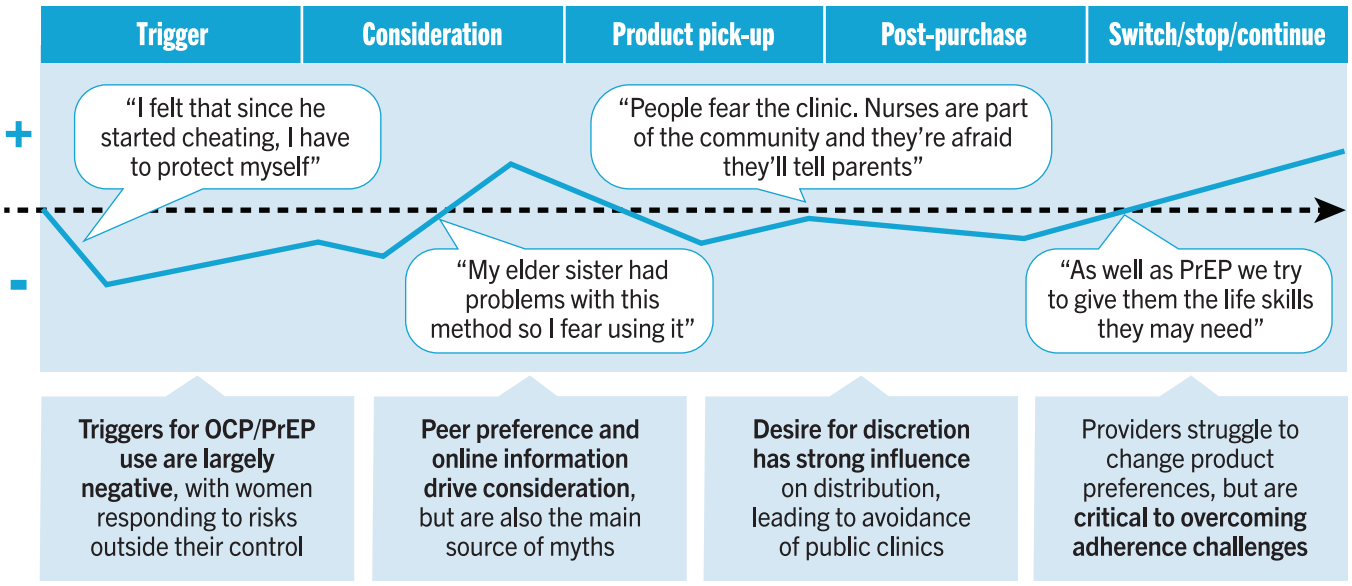
Figure 6: DPP user personas

DPP Persona		Description	Trigger Moment
	Elsie	Is **seeking enjoyment outside of her primary relationship** and prioritizes individual values such as enjoyment or career goals.	Discovered male partner having extramarital affair, then began her own affair to get even.
	Vicky	**New mother** who is motivated to use SRH products to perform this role, in a way that adheres to the social norms of motherhood.	After giving birth to her first child, wants to space births of subsequent children.
	Lindiwe	Wants to **maintain her romantic relationship**, in which she often has limited decision-making power and has to rely on her male partner.	Discovered partner was secretly living with HIV; does not want to lose security and social status that comes with a partner.
	Thandiwe	Has **experienced or is at risk of unintended pregnancy**, often compounded by low awareness of SRH options and limited locus of control with use of prevention products.	Unintended pregnancy postponed her plans to complete her studies and start a career.
	Faith	Has **unfaithful male partner** and is motivated to protect her health, but finds it difficult to negotiate safe sex with her partner.	Suspected partner of infidelity; wanted to protect herself without the need for her partner's consent.

The HCD research also identified the initial DPP user journey, based on where end users of OC/PrEP obtain information and form opinions on prevention, and how that impacts their decision-making. Male romantic partners and healthcare providers were found to play a key role in influencing women's decisions along their adoption journeys, and must be included in approaches to engage end users on the DPP. Key findings include:

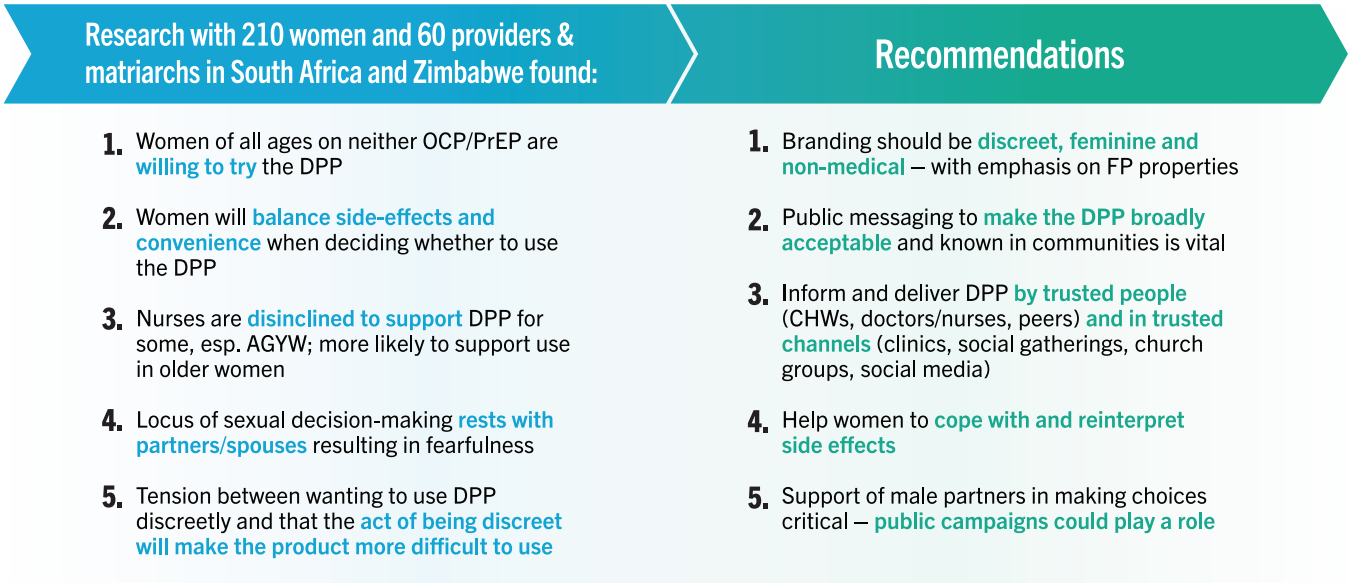
- **When deciding to use the DPP, women will have to navigate different sides of their identity and competing values.** They balanced a plurality of identities, e.g., independence, career goals and greater equality in sexual relations vs. appearance of respectability and religious, family and societal values. Relationship goals were connected to financial security and social status, and drove risk judgements in sexual health decisions. Women spoke openly and humorously about sex in the abstract, but only confided in one or two close friends about their personal lives.
- **Male partners warned the DPP could threaten societal gender norms, particularly older and rural men, but held more positive attitudes at an individual level.** Male attitudes were tied to identity – but this varied by social setting, e.g., talking openly and humorously with friends and supportive of their "side-chick" taking the DPP but less so for their female partner. Participants were personally supportive of the DPP, but some cautioned that this was dependent on their involvement in rollout.
- **Triggers for OCP/PrEP use were largely negative**, with women responding to risks outside of their control. For instance, nearly all PrEP journeys were triggered by an untrustworthy partner.
- **Peer preference and online information drove product consideration, but were also the main source of myths.** Many women supplemented provider advice with online product reviews, but this often reinforced rather than reduced confusion. Stigma and misinformation were likely to transfer between different prevention products.
- **Providers struggled to change product preferences of users, but were critical to helping them overcome adherence challenges.** Their influence often comes later in the user journey, dispelling myths and misconceptions, supporting women with discreet use and setting reminders, and serving as "life advisers". Because the DPP is a novel product, providers may have greater influence at the initiation stage, as they will be providing information on a product that will be new to all users.

Figure 7: Initial DPP user journey



Earlier HCD research conducted with 210 end users and 60 providers and matriarchs in South Africa and Zimbabwe[29] found that most women expressed interest in using the DPP, with slightly higher interest among women living in urban areas, yet they were concerned about: 1) side effects, as some women questioned whether a combined pill would have double or more intense side effects; and 2) ability to disguise the product from their partner. These findings were echoed in the more recent HCD research, pointing to areas that market introduction plans will need to address.

Figure 8: Key findings and recommendations from initial HCD research in South Africa and Zimbabwe



III. Our Approach

This section outlines the strategic approach that the DPP Consortium will pursue to plan for, introduce and scale the DPP in prioritized countries, beginning with an overview of the process followed by proposed approaches in thematic areas along the research-to-rollout framework.

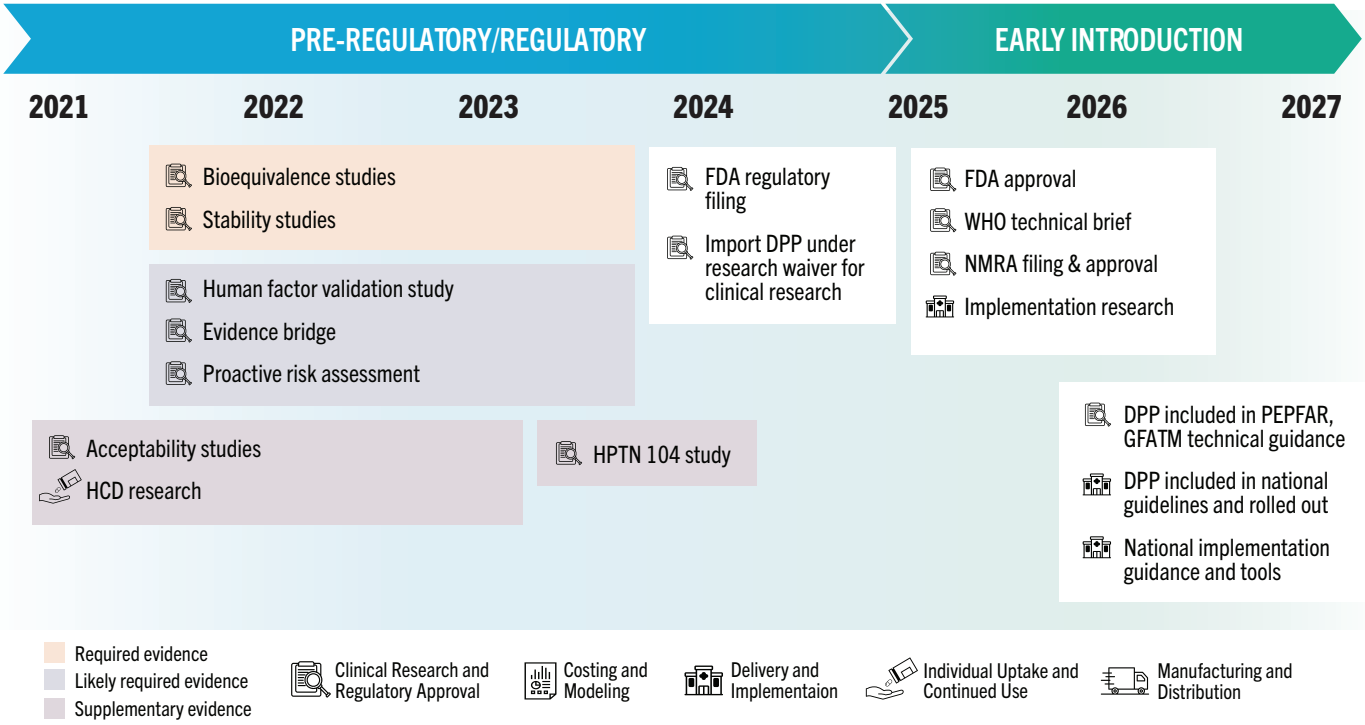
Recommended DPP regulatory and introduction pathway

1. Regulatory approvals and policies

Prior to FDA submission, Viatris will conduct bioequivalence (BE) studies to assess the DPP's equivalence compared to oral PrEP and COC alone. A proactive risk assessment, including a comprehensive, systematic evaluation of steps involved in using DPP, and a human factor validation study are also likely to be conducted per an FDA requirement to understand potential user errors, and an evidence bridge will likely be required to support the DPP submission with existing literature.

Viatris aims to file for regulatory approval with the US FDA in 2024 using a standard generic review pathway. Providing strong evidence to support DPP approval in lieu of a trial and early, extensive engagement with regulators and countries could accelerate time to rollout. Prior to or in parallel with FDA review, implementation partners can pursue IRB approval and import the DPP under a research waiver to be used in implementation research[iii] to speed real-world evidence generation, although permissions may vary by country. If funded and approved, clinical research (including acceptability studies using the co-formulated tablets) can start prior to FDA filing as long as the BE study is successful.

Figure 9: Regulatory pathway for the DPP



iii The terms "implementation research" and "demonstration project" are often used interchangeably. We use "implementation research" throughout this strategy, and nomenclature will be agreed upon as the project evolves.

Once approved by the FDA, projected for 2025, Viatris will pursue approval directly with multiple national medicines regulatory authorities (NMRAs) (the WHO Collaborative Registration Procedure is unlikely). In some countries, it may be possible to file with NMRAs while the FDA review is underway. Based on initial country landscape analyses, NMRAs in Kenya, South Africa and Zimbabwe are likely to allow for the BE of a fixed-dose combination product to be compared with the individual components of the product, as long as co-formulation of the two single-entity products is clinically justifiable under local regulations. A regulatory forum is planned in 2024 to better understand regulatory processes with NMRAs.

In 2025, the DPP Consortium will support the World Health Organization (WHO) to pursue an expedited review process for inclusion in global normative guidance, as the DPP is not an innovator product and thus will not require specific guidelines. When positive BE study results are available, the data, along with findings on user values and preferences from acceptability studies, consultations and any published research on the DPP, will be reviewed to issue a technical brief (similar to the approach with event-driven oral PrEP and the ring[30]). For the ring, the process from EMA opinion to WHO pre-qualification (PQ) took five months and was aided by strong backing from key stakeholders. WHO's recommendation of the dapivirine vaginal ring as one HIV prevention option for women at substantial risk for HIV acquisition was published three months after PQ. These are possible benchmarks for the WHO's review timeline, assuming the DPP has sufficient support from funders and the scientific community.

By 2026, positive BE results, stringent regulatory approval, acceptability studies, implementation research and WHO PQ will provide the impetus for inclusion in PEPFAR guidance and revisions to national guidelines. At country level, context-specific evidence on acceptability and impact modeling will accelerate funding allocations and inclusion in guidelines. A national coordination mechanism, likely established with country-level technical assistance and comprised of SRH and HIV prevention stakeholders including experienced end users, should review evidence and steer the guideline revision process, in alignment with other new HIV prevention products. Pilot studies will provide further evidence on cost-effectiveness, FP and HIV outcomes, demand and effective messaging to inform national implementation guidance and tools.

2. Regulatory review and early introduction

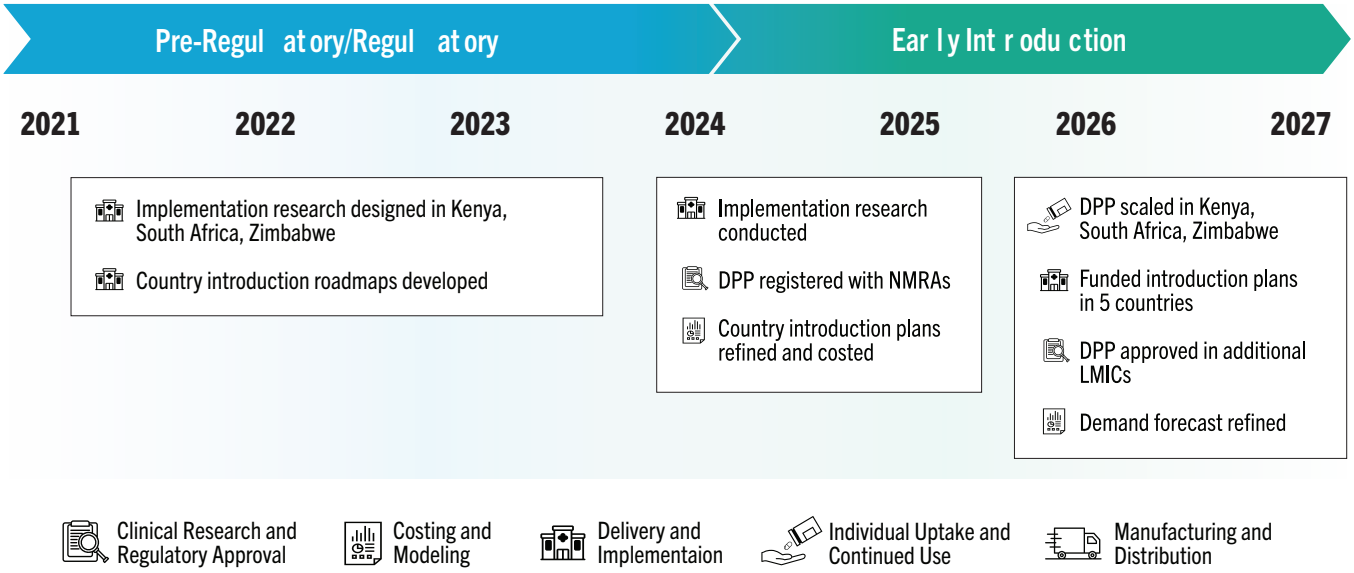
The DPP will be rolled out in a phased, evidence-driven process in countries that demonstrate interest and readiness to introduce the DPP and high potential for impact. Early introduction countries will be able to quickly build regional evidence, contingent on available funding.

Three countries have prioritized plans to design initial implementation research and undertake introduction planning in 2021-2024. Early evidence for scale-up will be generated in Kenya, South Africa and Zimbabwe, which were prioritized based on a scoping of need (identified as high HIV incidence and high unmet need for modern contraception, with geographic overlap of both); potential demand (indicated by high OC use) and enabling environment (defined by existing PrEP policies and investments allocated to scale national PrEP programs). More countries could be added with additional interest and funding commitments.

In parallel with market introduction planning, acceptability studies will be undertaken to provide early evidence on the DPP. Clinical cross-over acceptability studies in South Africa (n=96) and Zimbabwe (n=30), which are comparing adherence, acceptability and preference using an over-encapsulated DPP compared to two separate tablets (PrEP and COCs taken separately), will be completed in late 2023.[31, 32] The HPTN 104 study will be conducted with Viatris's co-formulated DPP in a similar cross-over study design with 1,000 women ages 18-35 across multiple sites.[33] HPTN 104 is expected to run from 2024-2025/6. Data from these studies will help to inform introduction and counseling strategies for the first-generation DPP once available.

Governments, through existing technical working groups (TWGs) or other national coordination mechanisms, will develop country introduction roadmaps with support from the DPP Consortium if needed. Roadmaps should include sub-national target-setting, prioritized service delivery channels and pre-regulatory adaptations. Recent oral PrEP decision-making (e.g., in South Africa) indicates that with technical assistance to support sub-national target-setting, the DPP could quickly scale. Assessment criteria for sub-national targets should look at: (1) high unmet need for FP and high HIV prevalence (and/or incidence where measured); (2) high OC use and high potential for total addressable market for contraception (TAMC) and (3) PEPFAR DREAMS districts, given high need, engagement of women ages 20-24 and linkages to SRH services.[34]

Figure 10: Regulatory approvals and early introduction of the DPP

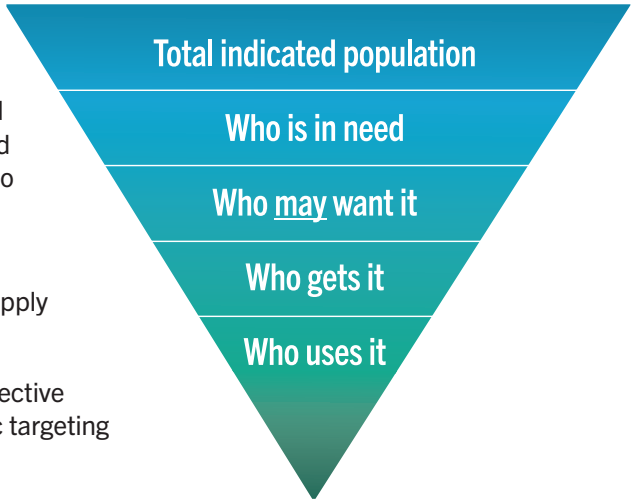


Implementation research is expected to begin by 2025 to rigorously assess acceptability, impact, cost-effectiveness and feasibility to deliver the DPP in different service delivery channels in Kenya, South Africa and Zimbabwe. The DPP Consortium will recommend additional countries for prioritization and partners will work with governments to support adoption of favorable policies, cost-effectiveness studies, target-setting, costing introduction plans and other critical activities, building the DPP into existing delivery platforms as feasible. With additional donor resources and favorable outcomes from implementation research, other countries that meet introduction criteria could roll out the DPP.

By 2027, the DPP should be scaled in Kenya, South Africa and Zimbabwe – assuming implementation research shows evidence of impact – with the goal of having funded introduction plans in at least 5 countries and regulatory approvals in additional countries. A preliminary analysis estimates 15 countries in SSA with HIV prevalence rates greater than 3% among women 15-49 have a potential total available market of 250,000-1.25 million DPP users per year.[35] However, these estimates do not factor in potential discontinuation rates, substantial growth in the oral PrEP market beginning in 2020, and PrEP ring and CAB for PrEP introduction. To hone this initial estimate to identify the target market, an evidence-based demand forecast for the DPP will be developed alongside other evolving HIV and FP product forecasts and will be continually refined based on:

- **Who needs it?** The total indicated population will be narrowed to identify who is in need of the DPP based on disease burden, risk profile and unmet needs.
- **Who may want it?** Ahead of introduction, based on planned end-user research and data from acceptability studies, need estimates can be refined to provide an initial estimate of who may adopt, via new use or conversion, the DPP.
- **Who gets it?** During early introduction, an uptake curve or demand forecast can be estimated based on clinical and supply considerations, implementation planning and user trends.
- **Who uses it?** Data on user characteristics, initiation and effective use will refine the demand forecast and steer programmatic targeting toward particular populations and service delivery settings.

Figure 11: Progressive demand forecast for the DPP



3. Implementation evidence generation

Implementation research will be designed in collaboration with governments and in consultation with advocates, end users, researchers, professional associations and other key stakeholders. It will initially be conducted in Kenya, South Africa and Zimbabwe, likely in public sector FP and HIV service delivery points, across urban and rural settings and among different segments of women, with aligned research protocols to allow meta-analysis and evaluate acceptability, impact, cost-effectiveness and feasibility. Private sector channels may be considered, contigent on authorization to prescribe oral PrEP in these settings. Funding opportunities across donors will be leveraged to pursue choice-based studies that offer the DPP with oral PrEP, CAB for PrEP and the PrEP ring to provide a nuanced understanding of user preferences in real-world settings. Implementation research design will build off of the lessons from the DPP acceptability studies and HPTN 104.

Primary implementation research partners will have track records of rigorous implementation research on HIV prevention and SRH, strong government and civil society relationships, established presence and reach in-country and across settings and experience with oral PrEP and FP introduction and delivering HIV and SRH services. Potential advocacy partners will include local advocacy organizations in Kenya, South Africa and Zimbabwe as well as regional advocacy coalitions. Civil society advocates, other community representatives and potential end users will contribute to shaping research engagement with women and communities. They will help build literacy, communicate results and advise governments and donors on implementation priorities to ensure community voices are represented through research and rollout. Advocates will raise awareness on and mobilize support for HIV prevention broadly as well as product-specific activities, including for the DPP, CAB for PrEP and the PrEP ring. Other partners (e.g., private sector, community-based women's groups) may be incorporated as the project evolves.

Research objectives are outlined in the following table. **Sub-studies will be conducted to inform scale-up** on cost/cost-effectiveness, utilization in different delivery channels, demand generation and provider motivators and barriers. Sub-studies on other objectives may be implemented with additional resources. Findings from implementation research will be used to influence national policies and scale-up, including around regulatory re-classification of PrEP to expand access, and to provide evidence for DPP rollout in other countries.

Figure 12: Primary and secondary research objectives for implementation research

Primary objectives	Secondary objectives
■ **Clinical outcomes** of the DPP (e.g., sero-conversions, pregnancy, adverse events, STI incidence). ■ DPP **initiation/effective use** across sites, channel types, other FP/HIV prevention methods, different segments of women. ■ **Provider motivators or barriers** to offering the DPP to a client. ■ **Cost/cost-effectiveness** of delivering the DPP in each setting. ■ **Optimal positioning** of the DPP vs. other FP/HIV prevention methods. ■ Impact of DPP introduction on **advancing HIV/SRH integration**.	■ **Strengthened platforms and lessons generated** for future MPT introduction. ■ **Characteristics and preferences** of women that initiate the DPP in each setting, including demographics and barriers/motivators to initiation. ■ Common **reasons for discontinuation or switching**, and support needed if HIV or pregnancy status changes. ■ **Training, supervision and other support** providers require to correctly deliver the DPP. ■ **Optimal clinic flow, mix of cadres, hours and areas of operation** to maximize client reach. ■ **Opportunities for task shifting** to lower-level providers and differentiated delivery approaches, such as HIV self-testing (HIVST).

4. Service delivery

Across countries, the DPP will be introduced and scaled in service delivery channels that have the greatest potential to reach women where they prefer to access services and are least stigmatized. In 2020, potential DPP channels were initially assessed based on: (1) alignment with user behaviors & preferences; (2) cost-effectiveness; (3) health systems readiness; (4) strength of M&E systems and (5) scalability.

The analysis found that **FP/MCH/SRH service delivery points** span client types and are a high-potential entry point for the DPP, as women are often introduced to FP (and to a lesser extent oral PrEP) in these settings through counseling, even if they are seeking other services, such as EC or post-abortion care.[36] **HIV clinics and PrEP delivery points** are best equipped to deliver the DPP, where providers are already trained to provide ARVs, though associated stigma and limited relevance for women who may not be as motivated to actively seek HIV prevention – typically not a primary concern – may limit reach. While **private sector and innovative channels** (such as telehealth and mobile clinics) may not be as ready to scale, they are often preferred by specific user groups, and those permitted to provide PrEP should be considered for implementation research. The PrEP landscape is quickly evolving – with a shift toward simplified, differentiated and demedicalized delivery for oral PrEP, including mobile, pharmacy and telehealth models as well as multi-month dispensing, indicating potential for diversified channels and provider cadres (types of health care workers) that could deliver the DPP in the future. **Additional channels should be considered for the DPP as soon as they are able to offer PrEP**.

a. Delivery channel selection in prioritized countries

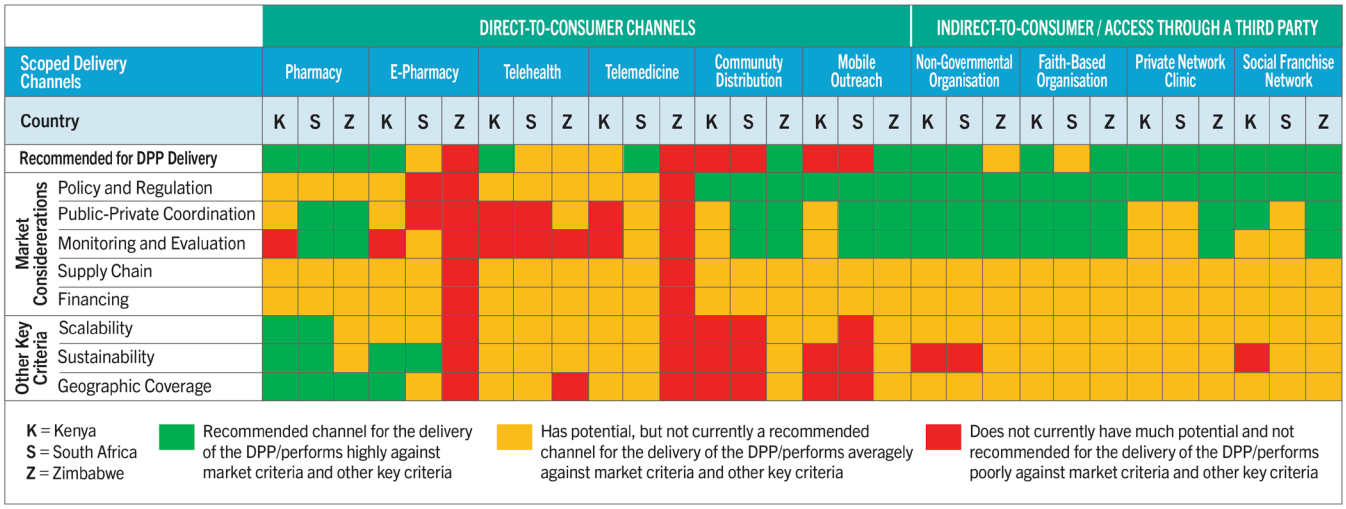
An initial analysis recommended that implementation research in Kenya, South Africa and Zimbabwe be conducted in public FP and HIV clinics, followed by scale-up in high-potential channels. An analysis of private sector channels completed in 2023 recommended including private sector channels in early implementation as well. As PrEP is decentralized, innovative and private channels with capacity to deliver PrEP and that have potential for impact and scale will be prioritized earlier. Governments will validate and ultimately determine channel sequencing in each country.

Figure 13: Service delivery channel sequencing in prioritized countries

Country	Phase 1 channels (2024-2025)	Phase 2 channels (2026-2028)
Kenya	■ Public FP/SRH clinics ■ Public HIV clinics ■ Private provider networks ■ Pharmacies, with links to other providers for prescribing ■ E-pharmacies	■ DICEs/Population-specific sites ■ Mobile clinics ■ Pharmacies, for both prescribing and dispensing ■ Telehealth
South Africa	■ Public FP/SRH clinics ■ Public HIV clinics ■ Private provider networks	■ DICEs/Population-specific sites ■ Mobile clinics ■ Universities ■ Pharmacies ■ Telemedicine
Zimbabwe	■ Public FP/SRH clinics ■ Public HIV clinics ■ Private provider networks ■ Pharmacies, with links to other providers for prescribing	■ DICEs/Population-specific sites ■ Mobile clinics ■ Universities ■ Pharmacies, for both prescribing and dispensing ■ Public-private partnerships ■ Community-based distribution

A DPP Private Sector Delivery Strategy was developed based on an updated scoping of private sector delivery channels in Kenya, South Africa and Zimbabwe.[37, 38] The research found that in all three countries, pharmacies exhibit high potential due to wide geographic reach, ongoing pharmacy-administered PrEP pilots in Kenya and South Africa and the ability to offer OC without prescription in Zimbabwe. Private networked clinics, which are already trusted for FP and HIV services and have systems to deliver these services in one place, also show promise. In Kenya and South Africa, newer, technology-based channels such as e-pharmacies and telehealth are rapidly becoming key entry points for many users due to nationwide accessibility, convenience and privacy, suggesting additional opportunities for DPP delivery. Findings are limited by a lack of standardized data for these newer channels and linkage to national M&E systems, as well as gaps in information on commodity pricing and willingness-to-pay for all channels. Preparing these channels for PrEP provision requires engagement with Ministries of Health and providers and further research on pricing and willingness-to-pay. Advocacy is needed to support policy shifts that include task-shifting for HIV testing, prescribing and refilling for pharmacists.

Figure 14: Analysis of market criteria for private sector delivery channels



DPP introduction will be expedited by pursuing channels that have integrated HIV/SRH services, task-shifted delivery of PrEP and already offer HIVST. In the pre-regulatory period, the DPP Consortium will work with countries to validate adaptations required for DPP delivery and link governments to appropriate, ongoing technical support in-country and through other co-investments. As the DPP moves closer to introduction, this strategy will be referenced to ensure delivery needs are addressed, including through existing investments in other HIV prevention products (CAB for PrEP; PrEP ring).

For instance, strong national mechanisms will be leveraged to coordinate and improve integrated service delivery, such as the HIV/SRH integration sub-committee in Kenya, PrEP and AGYW TWGs in South Africa and PrEP and SRH TWGs in Zimbabwe. Kenya, South Africa and Zimbabwe have conducive policy environments for DPP rollout, but more work is needed to integrate HIV/SRH services and systems.[39] Innovative approaches, including youth-friendly sites and oral PrEP pilots in FP clinics, can inform capacitation of the public sector to take PrEP to scale.

b. Clinical/quality strategy

Facilitating DPP uptake and continued use will rest on closer alignment between requirements for initiating OC and oral PrEP given different instructions for use, different standards for client follow-up across FP and HIV prevention and that OC delivery points are more aligned with women's preferences. Planning for DPP introduction will thus require:

Moving toward OC requirements that are clinically acceptable and responsible for oral PrEP.

- **Further simplify and streamline testing** to ease clinical monitoring (e.g., refills every 3 months, STI self-sample collection). HIV testing would follow national guidelines for PrEP prior to initiation and then every 3 months, which may be perceived as a barrier for current OC users. However, recent changes to WHO guidelines have relaxed HIV testing requirements, stipulating that HIVST can be used for initiation, continuation and re-initiation, support for social network HIV testing approaches and optional creatitine testing for people under 30 years old without kidney-related co-morbidities.[40, 41] Some implementation projects are assessing the feasibility of using HIVST to reduce clinic visits[42] and deliver HIVST alongside other SRH commodities, including PrEP, in private sector channels (e.g., Strengthening HIVST in the private sector (SHIPS) project).[43] Evidence shows young women like and prefer HIVST,[44] and community and peer-led distribution of HIVST has worked in South Africa and Zimbabwe.[45]

- **Sustain user-friendly adaptations to oral PrEP and FP delivery** such as multi-month dispensing (MMD), online follow-up and monitoring, task-shifting to lower-level provider cadres, HIVST and peer-led or assisted outreach, testing and adherence support – delivered closer to home. MMD should be offered after the first month where permitted. Distributing OC packs – and more of them – is associated with higher rates of effective use compared to OC prescriptions with more frequent return visits.[46] MMD every six months for oral PrEP with interim HIVST has been found to be non-inferior to quarterly dispensing and clinic-based HIV testing, with comparable adherence outcomes.[47] E-pharmacies are seeing an emerging demand for HIV prevention products; for example, MYDAWA sells 25% of HIVST kits in Kenya and is piloting oral PrEP delivery.[48] Making it easier for women to obtain the DPP across sites and channels, including via self-care platforms, and reducing clinic visits recognizes that some women are highly mobile and may access services at different delivery points.

Ensuring a high quality of initial counseling on the DPP. A provider counseling sub-group, comprised of global clinical experts with country-level expertise in HIV and SRH, developed initial counseling guidance messages to be tested in acceptability studies.[49] Messaging and related tools will be adapted to the needs of other channels, including pharmacies and social franchises supporting the private sector.

- **Providers must be equipped to support users to understand the product and benefits**, while decreasing the cognitive load of learning about two products at once. Providers must situate the DPP – a new product – within a range of prevention options and uphold informed choice.

- **Providers must be trained to support women through the pathway to care**, including screening and HIV testing, counseling, referrals for those that test positive for HIV and reporting. Initially, training and supervision may be funded and supported by donors and implementing partners. Longer term, technical support supervision for providers will transition to governments overseeing more diversified and integrated prevention programs.

- **Providers should be able to support women to anticipate and cope with side effects**, one of the most common reasons women stop using both OC and oral PrEP. Explaining potential side effects and how to manage them – without overemphasizing them – will be key. This includes changes to menstrual bleeding, a known concern for women.

- **Providers should spend time discussing potential for pausing, switching or restarting** – for instance, if a woman's fertility intention changes, if she dislikes the DPP but still needs dual protection or if her relationship status changes or induces a desire to discontinue her current method.

Figure 15: Summary of initial DPP provider counseling recommendations

Uptake: Take one pill every day for the DPP until the pack is empty. Days 1–21 contain COC and oral PrEP. Days 22–28 do not contain COC to allow for monthly bleeding, but do contain oral PrEP and pills should be taken to maintain HIV protection. Take the DPP for 7 consecutive days to reach protective levels against pregnancy and HIV.

Missed pills: If you miss 1 pill multiple times in a month or 2+ consecutive pills, take the DPP as soon as you remember. Do not take more than 2 pills in a day. If 2+ consecutive pills are missed, only take the last missed pill and discard the other missed pills.

Side effects: You may experience side effects when you start using the DPP, including changes to monthly bleeding. Side effects are typically mild and go away without treatment.

Discontinuation/switching: If you decide to discontinue use of the DPP, but want to be protected from HIV and/or unintended pregnancy, in most cases, you can begin using PrEP or another contraceptive method right away.

Drug interactions: There are no drug-drug interactions from combining oral PrEP and COC in the DPP. Certain medications are not recommended due to their contraindication with oral PrEP or COC.

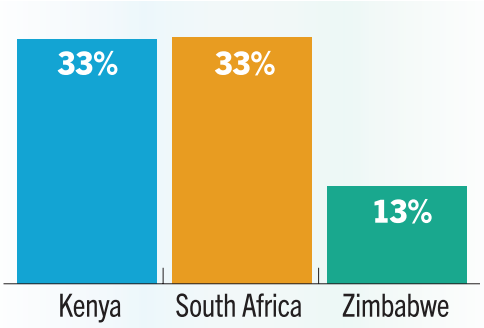
Monitoring: You will need to get an HIV test prior to initiating or restarting the DPP, and every 3 months during DPP use. Your provider may recommend other screening or testing (i.e., for STIs or pregnancy).

This is a topline summary of the recommendations. Complete recommendations and supporting evidence are available here.

Establishing a level of support for follow-up, including use of peer outreach and mHealth. Acceptability studies and implementation research will offer insights on end-user preferences and successful approaches for follow-up.

- **Women that discontinue or switch** methods as fertility intention or risk change will require more support than typically provided in FP programs. Discontinuation is common among OC[50] and oral PrEP[51] users. Decision support tools have been developed to support informed choice for FP methods[52] and as self-assessment tools for oral PrEP initiation.[53] Implementing partners are revising these tools as more HIV prevention options become available and employing them in implementation research.[54] The DPP should be integrated into both FP and PrEP decision making tools, which could help women to assess which method would work best for them.
- **Identify the level of follow-up required** if a client does not return for a refill based on counseling and any barriers to access that may have been discussed. FP and HIV approaches diverge, with FP taking a more passive approach and the majority of clients discontinuing a method on their own. Oral PrEP and ART follow-up tends to be more proactive and resource-intensive.

Figure 16: Annual discontinuation rates of OC while in need



FP2020 Core Indicator Summary Sheet: 2019-2020 Annual Progress Reports for Kenya, Zimbabwe; South Africa Demographic and Health Survey 2016.

- **Level of follow-up should be as close to FP support as possible to minimize provider and client burden** while building on existing HIV infrastructure and successful oral PrEP support interventions, such as peer outreach and mHealth.[55] These include early identification of women who may be at greater risk of discontinuing, contacting women who miss a refill or digital reminders to take pills, which could also help identify those inclined to discontinue the DPP. This may be a new experience for oral PrEP-naïve users, requiring explaining upfront.

- **Integrate the DPP into existing mHealth applications** – outreach, educational and counseling messages, decision support tools and reminders for refills via mobile phones – which are effective at keeping women engaged in FP and HIV services.[56] Digital platforms can use nudges and rewards to promote long-term positive behaviors, as Triggerise does, and offer increased channels for communication, for instance via WhatsApp and hotlines, as seen with Kasha.

c. Provider training/provider demand generation

Based on a review of policies on oral PrEP and OC provision, nurses are currently the lowest level cadre with the highest workforce coverage eligible to prescribe and dispense the DPP across prioritized countries. FP nurses will need training on oral PrEP and may require support to manage additional burden to their workloads. ART/PrEP-certified nurses may need refresher training on FP and training on how to counsel and support women to use a combined product. Qualified cadres in the private sector will need to be integrated into training programs targeting public providers.

Figure 17: Summary of cadres' ability to prescribe and dispense OC and PrEP by country

	KENYA		SOUTH AFRICA		ZIMBABWE	
	Prescribe	Dispense	Prescribe	Dispense	Prescribe	Dispense
OC	Doctors Nurses Midwives *Pharmacists are not allowed to prescribe but often dispense without a prescription*	Doctors Nurses Midwives Pharmacists CHWs *(refills only)*	Doctors Nurses Pharmacists with expanded FP permit	Doctors Nurses Pharmacists	*No prescription required*	Doctors Nurses Midwives Pharmacists CHWs *(refills only)*
Oral PrEP	Doctors Nurses Midwives Clinical Officers	Doctors Nurses Midwives Clinical Officers Pharmacists	Doctors NIMART* trained nurses Nurses with PIMART** permit Pharmacists with PIMART** permit	Doctors Nurses Pharmacists	**Public sector:** Doctors Nurses trained on HIV care and treatment **Private sector:** Doctors	Doctors Nurses Pharmacists

* NIMART – Nurse Initiated Management of Antiretroviral Therapy
** PIMART – Pharmacist Initiated Management of ART (currently on hold)

To maximize delivery and preempt stigma around the DPP, providers and governments should:

Advocate for policy changes and support expanded trainings to task-shift PrEP delivery to pharmacists, community health workers (CHWs) and other cadres, supporting efforts that are underway to align with OC provision and expand viable DPP service delivery points. Advocacy partners must be sufficiently funded as their engagement with government decision-makers is critical for designing prevention programs that best serve users and communities.

Support women to use self-testing for HIV and pregnancy, including via co-delivery of self-test kits, and capacitate peer navigators/lay workers to do testing, counseling and referrals to offset provider workloads, especially in large tertiary hospitals.

Incorporate provider-focused behavior change interventions into clinical training, as some nurses may be disinclined to support the DPP for younger women, who they believe cannot be trusted to take daily oral pills, but would support the DPP for older women, who they see as more responsible and who may want the flexibility of an OC.[57] Poor product knowledge of oral PrEP among providers is an added barrier, though oral PrEP scale-up can begin to build their literacy now.[58] Values clarification training and a supportive environment can address provider bias.[59]

Adapt clinical mentorship programs and provider communities of practice to support provision of the DPP. Mentor models/champions have helped build provider capacity to deliver integrated HIV/SRH services.[60]

5. Promotion/demand generation

a. Branding the product

Building off the oral PrEP experience and a range of HCD and market research, **the DPP will be branded with a lifestyle feel**, as a product women can integrate into their daily routines.[61] HCD research on the DPP found that women want branding and packaging to be discreet, feminine and non-medical, with no obvious references to HIV or oral PrEP, as perceived association with HIV is stigmatizing and will likely dissuade use. Women respond positively to branding that feels relevant and familiar, and products that instill confidence and self-efficacy.

Viatris is opting for a wallet-pack structure for the DPP with sheets that tear off a week of blister-packed pills, which will more closely resemble OC packs. This decision responds to an aversion to products that look like oral PrEP or ARVs and that are less discreet, such as pill bottles. Viatris has selected a global brand name based on research with end users in South Africa and Zimbabwe. Focus groups will be engaged to assess women's viewpoints and preferences to ensure that the branding design reflects their inputs.

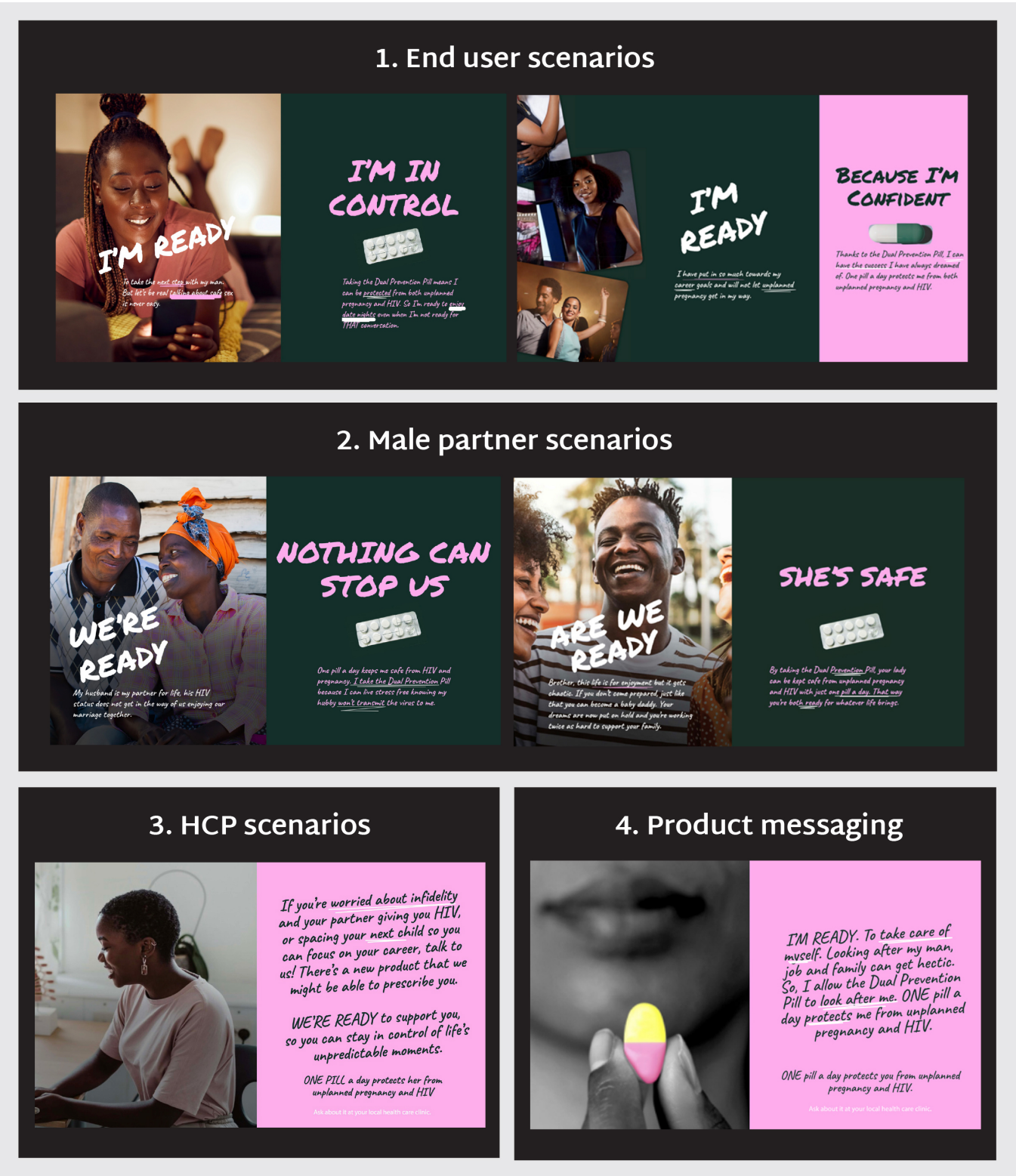
b. DPP positioning

HCD research in Kenya, South Africa and Zimbabwe revealed the following key themes that shaped initial positioning for the DPP:

- **Connect the DPP with women's diverse identities and goals**: For women to want to take the DPP, it is not enough for them to believe in the functional health benefits of the product. Women need to believe that the DPP also aligns with their values, beliefs and identities, and that they can take the pill without facing social repercussions. When deciding to use the DPP, women are likely to negotiate different sides of their identity and competing values. Many struggle to balance personal, self-focused motivations related to enjoyment and career goals with performing a respectable, traditional role in certain relational and societal contexts. Women felt motivated when their individuality was celebrated, whether through a goal-oriented, enjoyment or self-care lens, and when taking the DPP did not risk damaging their social status or reputation. There is an opportunity to show that the DPP can help women navigate the competing values in their lives.
- **Link the DPP with relationship goals**: The risk of damaging a relationship often felt more immediate and was a stonger influence on end users' behavior than health risks such as HIV, which many discounted because it felt distant or "wouldn't happen to me." This was particularly significant given the personal and social status attached to being in a relationship and the importance placed on family values. OC and PrEP were seen as products that could put relationships at risk, including because they signaled that women do not trust their partner or are cheating on them. There is a role for communications to flip this perception, showing that DPP users care about their partner and protecting their relationship. Men liked being positioned as "protectors" of women in their lives as a way to engage them on support for the DPP and connect with gender norms.
- **Leverage different triggers for media targeting**: Most triggers to OC and PrEP use related to negative experiences, with the majority of PrEP users citing an untrustworthy partner. Women strongly identified with the type of person who is prepared to take on risks that are often outside their control. These "trigger moments" are significant entry points for the DPP that can be targeted through media placement, positioning the DPP as a product that can help women navigate moments when they need to take control of their sexual health.

These findings led to the development of a creative concept – *I'm Ready* – centered around the message that the DPP could help women prepare for the unpredictability of life. This direction reflected the findings that being "ready for anything," in particular the actions of their romantic partners, resonated more strongly with end users than actively seeking to prevent HIV. The concept performed best when it connected to everyday moments and supported women to achieve career and family goals. Men appreciated executions that framed them as "in it together" with their female partners but were less supportive when the route challenged traditional gender norms. Based on these findings, the DPP was positioned as a product that could instill confidence in women that nothing will get in the way of living the lives they desire. Creative materials will be adapted to local country contexts and piloted in implementation research.

Figure 18: Examples of "I'm Ready" creative stimulus tested in validation workshops



c. Demand generation strategy

Both recent and previous HCD research found a resounding need to raise public awareness on the DPP to create social acceptability. Women acknowledged the tension between desiring a product that promoted discretion and hoping that public campaigns to make HIV prevention and contraception use "popular" (and the DPP specifically where marketing regulations allow) would help eliminate the need to have to be discreet. At the same time, safe and trusted channels should be leveraged for more targeted communications to specific audiences for messaging that could be seen as more controversial with male partners and wider communities.

HCD workshops conducted with end users, male partners and healthcare providers in Kenya, South Africa and Zimbabwe revealed several insights that will inform the development of a comprehensive DPP demand generation strategy:

- Lean into the normalization of talking about taboo topics that affect women by using the place of promotion strategically to provoke interest (e.g., public spaces for some messages). However, these topics need to be framed sensitively and delicately to resonate with target audiences, for example, when discussing infidelity.
- While making the most of private and targeted spaces, there is confidence a campaign launch in public spaces would promote positive discussion.
- Include a variety of messages not related to women's relationships and dating lives that speak to their appreciation for empowerment, including on self-care and life goals. Aim for inclusivity in messaging, considering different end users and moments in their lives (e.g., reframe "husbands" to "partners" to encompass women in relationships who are not married).
- Ensure that messaging is unambiguous. The DPP is a novel product and audiences want to clearly understand its components and what it does. Messaging that framed the DPP as "OC-plus" and downplayed the PrEP component of the product was not well-liked and caused confusion, underscoring the need to be clear that the DPP contains PrEP despite the potential for associated stigma.
- Position men as protectors of women in their lives, particularly those who are not their romantic partners (e.g., female friends and relatives), as their desire to act as a protector to women overtakes reservations they have around sexual health conversations and products. Capturing the shared experiences of men, particularly those focused on enjoyment and fun, could provoke discussions among their peers to help change the negative perception men currently have around sexual health products.
- Position providers as relatable and supportive of the priorities of women to help their clients feel confident. Equip providers with tools to support continued use, such as apps and packaging that promote discretion, which is especially important to end users.

d. Community and influencer engagement

HCD research highlighted the need for broader engagement of influencers and communities to lay the groundwork for DPP introduction, given their role in the SRH decision-making of end users. Strategies include:

- **Leverage trusted members of their network as advocates for the brand**: Across Kenya, South Africa and Zimbabwe, women spoke of having one or two close confidants that they would go to for information and advice about SRH. Typically, this is a close friend or older sister who has been through a similar journey navigating sex, relationships and use of SRH products. In more rural settings, women often received advice from aunties, sengas or mamacanes (mother's younger sister) due to more closed conversations with their mothers. These members of women's networks could be cultivated as advocates and champions for the DPP, positioning them as trusted sister or aunty figures who can provide anonymous support and advice to end users. Equally, end users can be encouraged to share information about the DPP with their confidants, e.g., providing them with social media or WhatsApp content they can pass on to those they care about and want to protect. At the community level, messages about the DPP could be cascaded through trusted members of the community, such as community and religious leaders.

- **Turn supportive male partners into advocates for the brand**: At the societal level, there was significant male resistance to the idea of the DPP, for instance because it could be seen to give women greater license to cheat on their partner and therefore threatened masculine gender norms. However, at an individual level, many men (particularly younger, urban individuals with a higher socio-economic background) recognized that their extra-marital affairs put their partner at risk and expressed more supportive attitudes towards the DPP. To increase the acceptability of the DPP among men, communications targeted toward men could position the DPP to align with their values and beliefs, and include reassurances and myth-busters to counteract fears about the effect of the pill on fertility and libido. Men who are individually more supportive of the DPP could be promoted as champions for the product.
- **Shift perceptions about who is likely to take the DPP**: Although many research participants held more positive opinions about OC and PrEP users at an individual level, all noted the widespread social stigma that persists, with women on PrEP associated with promiscuity and pre-marital sex. To increase the social acceptability of the DPP, there is a need to counteract existing negative perceptions and build a new set of positive associations around those taking it. Suggestions made by research participants included associating the DPP with women who are thinking of their children's futures or their own career, or who are health-conscious and savvy about protecting themselves from male partners' risky behaviors.

In addition to these engagement strategies, the DPP Civil Society Advisory Group was launched in 2021 to guide DPP research and market introduction plans. The group, comprised of 14 advocates from Kenya, South Africa, Uganda and Zimbabwe, meets periodically to ensure that civil society perspectives are embedded in DPP planning and that advocates are up-to-date on DPP progress to support their advocacy on SRH.

6. M&E

Given significant variability between oral PrEP and OC program measurement, it will be crucial to drive early consensus on critical DPP indicators for routine monitoring, as well as a wider set of indicators better suited to generate early evidence to inform scale-up through enhanced monitoring systems and implementation projects. Findings and initial insights documented through a review of existing FP and HIV prevention M&E systems can inform priority next steps for country-level M&E planning and key areas where differing practices across HIV prevention and FP will need to be reconciled to ensure data visibility for the DPP and other MPTs.[62]

Usage and impact of oral PrEP can be estimated with: (1) new initiations; (2) follow-up visits and (3) re-starts, if those indicators are collected and data is available at that level of disaggregation. However, parallel data systems and inconsistent indicators across partners and programs (e.g., UNAIDS, PEPFAR, WHO, country programs) remain common, creating challenges for data availability as well as longer term sustainability. Moreover, many programs leverage HIV-specific M&E platforms, which may limit data visibility across expanded PrEP or DPP delivery channels that are not traditional ART delivery sites.

In contrast, FP indicators are widely integrated into national health information systems and regular demographic health surveys, enabling strong data visibility and comparison across countries. FP usage estimates are generally extrapolated from commodity distribution (HMIS, LMIS) and global and national surveys (UNFPA facility, PMA, DHS), with key indicators including: (1) couple-years protection (CYP); (2) stockouts and (3) method availability. Coordination through global initiatives, such as FP2030 and PMA, has supported adoption of these consistent, validated indicators. However, there is a heavy reliance on CYP. While this indicator provides a consistent measure across products, it does not capture nuances of product use, client satisfaction or choice, which will be crucial for understanding the role of the DPP and other MPTs in the method mix. It is also conceptually complex.

To ensure health systems are well-positioned to support effective DPP M&E, additional country-level engagement is needed to:

- **Establish a shared definition of "success" for DPP introduction through engagement with government stakeholders as well as communities**. Aligning on a shared view of success will be essential to determining priorities for evidence generation and ongoing monitoring. This should be an iterative process, as definitions of success may shift with changing dynamics in FP and HIV prevention.
- **Identify a minimum set of critical indicators** for national systems to support target-setting, impact measurement and clinical monitoring across HIV prevention and FP programs. Experience from HIV prevention has demonstrated that a lack of early coordination and alignment on these indicators can contribute to delays in wider scale-up due to poor data visibility.
- **Align on evidence generation priorities to address through enhanced monitoring systems** in research studies and implementation projects. While FP provides a model for well-coordinated, sustainable M&E, routine systems are not well-prepared to address all evidence needs for MPTs, such as continuation rates and product switching. In HIV prevention, longitudinal studies have been crucial for understanding reasons for discontinuation, as well as barriers and enablers for uptake; however, as with FP, these metrics are not included in routine monitoring systems to avoid overburdening providers. This highlights the need to leverage enhanced monitoring mechanisms and evidence generation through implementation projects rather than attempt to meet evidence needs through routine data collection.
- **Identify requirements, processes and timelines for including new indicators in national M&E systems**, engaging stakeholders involved in HIV prevention, FP and health information system management. This should also include mapping the processes for integrating MPT indicators into the FP platforms not currently used for HIV prevention, such as the DHS, to ensure systems are well-positioned to track and monitor the role of the DPP and other MPTs in the FP and HIV prevention method mix.
- **Conduct country-level mapping of provider M&E capacity**, including existing data collection processes, training mechanisms and process to support data collection, and timelines and requirements for revising training curricula and tools for new data collection processes.
- **Support early collaborative planning between partners and Ministries of Health on M&E approaches, knowledge management plans and research objectives in early implementation projects** to drive co-ownership of the research agenda, early alignment around more resource-intensive methods for implementation projects and to ensure research projects are capacitated to help identify and validate the minimum package of critical indicators.

To help speed up inclusion in M&E systems, the DPP Consortium will work through complementary projects to **support country efforts to strengthen and align national M&E systems across HIV and FP programs**, with a move toward electronic monitoring systems, prior to DPP rollout, as is feasible given specific country contexts. Importantly, these efforts should establish best practices and update protocols to accelerate inclusion of future MPTs.

7. Supply Chain

The current manufacturing capacity is expected to be sufficient for at least the first three years. Viatris is expected to be able to produce a supply for 250,000+ women per year, and may be able to increase capacity further with additional packaging equipment. As demand becomes clearer, needed capacity will be reassessed and additional manufacturers may need to be engaged to enter the market to increase supply and enable scale. LNG/EE can only be manufactured in dedicated hormonal facilities, so ideal manufacturers will already be manufacturing an LNG/EE OC product. In the meantime, in the context of a single supplier, early consideration and ongoing risk assessment will be critical to identify potential challenges in advance, ensuring supply security and addressing concerns from governments and procurers.

While the cost of the DPP compared to other HIV prevention and FP options suggests that the product may be procured primarily by HIV-focused agencies, depending on country contexts and priorities, impact will likely require delivery in public sector FP programs and via private sector partnerships. This will require early, extensive coordination to align separate HIV/FP target-setting, quantification, procurement plans, funders and intervention costs at country level.

Though some HIV donors, such as PEPFAR, have not purchased contraceptives to date, the DPP may be an opportunity to explore this. Both statute and regulations permit that PEPFAR may procure HIV/AIDS pharmaceuticals and ARVs which appear on the PEPFAR Consolidated List of Approved ARVS. However, this has not yet been interpreted in the light of an ARV-containing MPT which is both an 'HIV/AIDS pharmaceutical' and a contraceptive. Initial analysis suggests that clarifying the US government (PEPFAR, USAID) approach to MPT procurement should be a priority for early engagement.[63]

Alongside further engagement to understand requirements and evidence needs from major procurers, assessing opportunities to integrate the DPP and other MPTs into existing global coordination mechanisms will be important. These include the ARV Procurement Working Group (APWG), which facilitates coordinated procurement of low-volume products through quarterly order placement cycles, and the Global Family Planning Visibility and Analytics Network (GFPVAN). With multiple new HIV prevention products heading to market, including CAB for PrEP and the PrEP ring, there may be a need for a prevention-focused sub-group of the APWG, which could provide an important body for coordinating DPP procurement. As DPP development progresses, engaging key FP stakeholders, such as the Reproductive Health Supplies Coalition, FP2030 and UNFPA, as well as HIV stakeholders will be important to consider and assess the value-add of a coordination platform for MPT procurement.

National procurement and planning processes will require tailored strategies for engagement.[64] For HIV commodities, South Africa contributes significantly to funding and is now the largest procurer of condoms in the world,[65] whereas Kenya and Zimbabwe rely more on donor funds. National supply chain management systems and public sector supply chain agencies will need to bridge traditional HIV and FP channels to ensure the DPP and ancillary products, such as HIV testing (in FP clinics) and pregnancy tests (in HIV clinics), can be reliably supplied to prioritized distribution points. As HIV and FP commodities are procured through separate supply chains in many countries, it will be crucial to begin supporting integration through targeted technical assistance in advance of product availability. Measures will need to be put in place to guarantee women uninterrupted access to OC/FP and oral PrEP as a stopgap in the event of a DPP stockout.

Social marketing organizations (SMOs) should continue to be explored as a complementary avenue for procurement, as they can support targeted delivery of the product to the potentially niche consumer base for the DPP. SMOs can also be nimble and responsive, supporting diversity in how clients can obtain FP commodities. Moreover, in contexts where large proportions of the population access FP services through the private sector, SMOs may be an important delivery channel.

IV. Funding required and financials

1. Initial introduction

a. Cost estimate

The DPP will be advantageously positioned to scale if the cost is at parity with the combined cost of oral PrEP and COC, or, ideally, even lower. The current price of generic daily oral PrEP is approximately $46/year (see Global Fund ARV Reference Pricing and USAID Product e-Catalog), while the cost of daily COC is about $4/year. Based on an initial cost of goods (COG) analysis conducted by CHAI as part of the DPP Consortium, it may be feasible for the DPP to reach parity or a lower price than the current combined price of separate oral PrEP and COCs.[66] However, generic pricing ultimately depends on a range of factors, including volumes, buyer pricing tolerance, the broader FP and HIV prevention product landscapes and whether additional suppliers are preparing to enter the market, among others. This analysis will be refined as more data becomes available.

b. Initial value for money estimate

HIV funders may be encouraged to invest in the DPP if cost-effectiveness and end-user preferences are clear, especially given the ongoing introduction of the PrEP ring and CAB for PrEP in locations where injectable contraception tends to be prioritized by many programs, providers and users. In advance of more rigorous cost-effectiveness modeling, **an initial value for money analysis of high-level DPP-related cost and impact outcomes informed continued and co-investment for DPP introduction planning**. The analysis estimated directional financial savings from product co-formulation and service delivery integration as well as unintended pregnancies and primary HIV infections averted over a one-year snapshot of DPP use at a set number of annual users. The analysis did not include product introduction and start-up costs such as initial training or system changes, model costs or impact over multiple years, estimate secondary and tertiary HIV infections averted or examine detailed cost-effectiveness outcomes. Additional cost savings from avoiding lifelong ART and HIV labs and unintended pregnancies are an "additional upside" but were not included in the analysis.

While the initial value for money analysis provides an estimate of directional financial savings, inputs and assumptions, including (1) adherence to PrEP; (2) adherence to OCs; (3) DPP adherence; (4) commodity cost reduction at scale and (5) personnel cost, reductions are expected to vary by country and will heavily shape the outputs of this analysis. **Impact estimates** assess unintended pregnancies and primary HIV infections averted. For HIV prevention, ensuring access for women who are at high risk of infection (based on estimated HIV incidence) and supporting adherence through counseling and outreach will increase the impact of the DPP. With improved adherence and messaging about the enhanced benefits of a dual product, the DPP may have more impact on preventing unintended pregnancies. **Cost savings** estimates suggest that even with modest decreases in cost as compared to the individual products (i.e., DPP parity with oral PrEP), the **primary driver of direct cost savings will be reduced commodity costs due to co-formulation at scale**. Additional marginal savings may be gained due to integrated delivery of HIV and SRH services. The analysis does not account for product introduction and start-up costs, such as initial training and system changes; these costs will likely decrease overall savings.

c. Cost-effectiveness modeling

CHAI, in partnership with NYU, conducted preliminary cost-effectiveness modeling to understand the potential impact of DPP introduction. Outcomes were measured in HIV infections averted and unintended pregnancies averted, as well as a combined health outcome measure (DALYs averted). The modeling approach was informed by extensive consultation with the DPP Consortium to align on priority research questions and appropriate product assumptions. Modeling results from Nyanza (Kenya), South Africa and Zimbabwe indicated the DPP is more likely to be cost-effective in populations with the highest risk of acquiring HIV. The DPP was found to be cost-saving in some populations (e.g., sero-discordant couples in Kenya and South Africa, FSW in South Africa and Zimbabwe).

Results also demonstrated cost-effectiveness is highly sensitive to user adherence: if the DPP leads to increased adherence among those using oral PrEP with low adherence rates, the DPP is more likely to be cost-effective. On the other hand, the DPP has the potential to be net-harmful if it reduces adherence among some OCP users. This finding is driven by the high relative importance of FP outcomes in overall health outcomes (measured by DALYs averted) and the declining background HIV incidence across study settings. As such, gathering real-life data to understand the impact of the DPP on adherence will be critical and should be a priority for early implementation research to build evidence for adoption and investment decisions.

Based on the modeling findings, CHAI and NYU refined modeling to include additional FP inputs and conducted further analysis to determine the adherence thresholds at which the DPP remains net beneficial, finding that the DPP is net-beneficial across most populations and scenarios, even at relatively low adherence. The DPP is cost-saving among FSW in South Africa, even with relatively low adherence (19%) and cost-saving among serodiscordant couples in South Africa and Nyanza with moderate adherence (>75%). However, results underscore the dependence of cost-effectiveness on high background HIV incidence; among populations with lower background HIV incidence (women aged 25+ in Nyanza and AGYW in Nyanza and Zimbabwe), minimum adherence must be above 60%. Further modeling will be needed once study and real-life data is available on delivery costs and adherence rates.

d. Financing

Funding for the DPP is likely to derive from existing HIV prevention budgets, given that the oral PrEP component is the main commodity cost driver. However, expenditures for HIV prevention are currently far below estimated resource needs and prevention budgets are highly constrained. In 2019, an estimated USD $5.2 billion was spent on primary prevention — estimated resources for primary prevention in 2025 are nearly double that, at USD $9.5 billion. As of 2020, PEPFAR allocated USD $35.7 million to PrEP and has historically been the largest PrEP payer; however, the total global PrEP funding for that year is not yet available.[67] The Global Fund is expanding its remit to include support for broader SRH interventions, and could be a funding source for the DPP. HIV care and treatment has taken a growing piece of the absolute budget for HIV funding, driven by the cost to support ever larger numbers of people enrolled on ARVs. Consequently, a growing number of HIV prevention interventions are vying for a shrinking piece of the funding pie.

While domestic financing is expected to remain low, there is a growing pressure for countries to finance the procurement of FP commodities. The South African government, which manages the largest national HIV response in the world and covers 75% of resource needs through domestic funding, could potentially finance the DPP.

FP donors may provide some degree of underlying infrastructure and service delivery funding, but are unlikely to pick up the substantively higher cost of oral PrEP in order to offer the DPP, especially in the current context of a shrinking FP funding landscape.

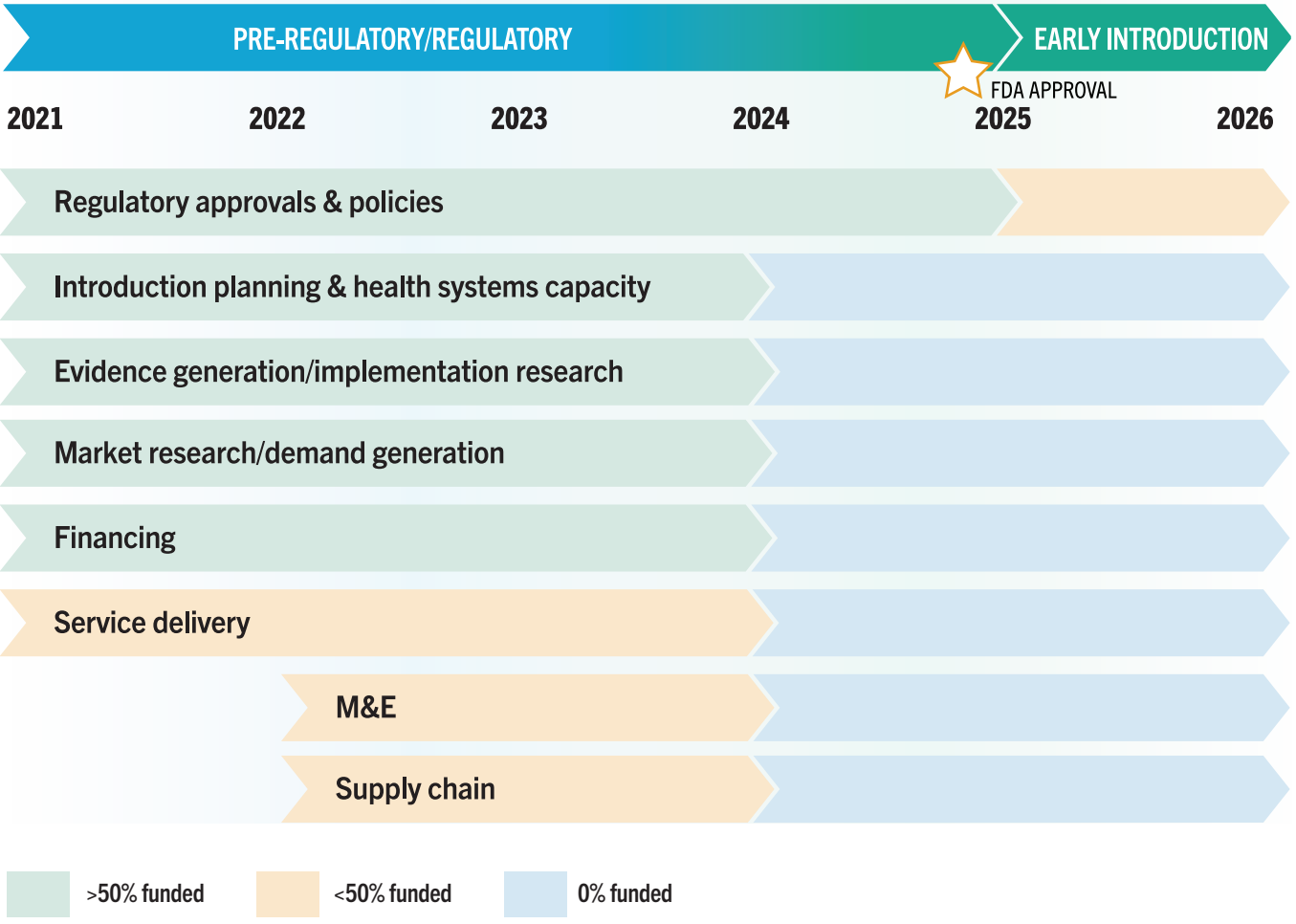
User willingness to pay will be low given oral PrEP is currently distributed for free, and generic Ocs are affordable for much of the population. In this context, introduction of the DPP into the private sector will likely require significant subsidization of the DPP to near-parity with OC, which will likely set the pricing bar for consumers.

2. Critical introduction activities

From 2021-2026, activities across the research-to-rollout framework will be critical to facilitate rollout of and access to the DPP. Based on initial cost estimates of market preparation and introduction activities, a significant portion of funding for pre-regulatory/regulatory activities has been secured or is anticipated, though as of this writing early introduction activities are primarily unfunded. These cost estimates do not include investments in product development.

The graphic below is a high-level snapshot of the approximate funding status of activity categories, which bundle the activities described in the preceding sections of this document. The table will serve as a reference when coordinating investments and tracking activity progress, including opportunities to integrate with or leverage complementary projects to fulfill needs.

Figure 20: Estimated funding for critical introduction activities for the DPP



V. Annex

1. List of Acronyms

AGYW	Adolescent girls and young women	**LNG/EE**	Levonorgestrel and ethinyl estradiol
APWG	ARV Procurement Working Group	**M&E**	Monitoring and evaluation
ART	Antiretroviral treatment	**MCH**	Maternal and child health
ARV	Antiretroviral	**MMD**	Multi-month dispensing
BE	Bioequivalence	**MPT**	Multipurpose prevention technology
CAB-LA	Long-acting cabotegravir	**NGO**	Non-governmental organization
CBD	Community-based distribution	**NMRA**	National medicines regulatory authority
CHAI	Clinton Health Access Initiative	**OC**	Oral contraception
CHW	Community health worker	**Oral PrEP**	Oral pre-exposure prophylaxis
CIFF	Children's Investment Fund Foundation	**PEP**	Post-exposure prophylaxis
COC	Combined oral contraception	**PPP**	Public-private partnership
COG	Cost of goods	**PQ**	Pre-qualification
DICE	Drop-in center	**PrEP**	Pre-exposure prophylaxis (all delivery forms)
DPP	Dual Prevention Pill	**SRH**	Sexual and reproductive health
EC	Emergency contraception	**SSA**	Sub-Saharan Africa
FDA	U.S. Food & Drug Administration	**STI**	Sexually transmitted infection
FP	Family planning	**TAMC**	Total addressable market for contraception
FSW	Female sex worker	**TDF/FTC**	Tenofovir disoproxil fumarate with emtricitabine
HCD	Human-centered design	**TWG**	Technical working group
HIVST	HIV self-testing	**WHO**	World Health Organization
LARC	Long-acting reversible contraceptive		

2. Figures

Figure 21: Cross-country factors for DPP potential in SSA

Metric	Kenya	South Africa	Zimbabwe	Eswatini	Zambia	Botswana	Malawi	Lesotho	Nigeria	Uganda
HIV prevalence rate (15-49, all women)[68]	4.9%	23.5%	13.7%	35.2%	13.8%	21.2%	8.9%	24.3%	N/A	6.5%
Unmet need for FP (15-49, all women)[69]	12%	11%	8%	9%	15%	8%	13%	9%	15%	16%
OCP use (% of method mix)[70]	9.9%	10.5%	26.9%	12.3%	14.4%	4.9%	3.7%	21.5%	11.4%	5%
Year oral PrEP approved[71]	2015	2015	2017	2017	2017	2016	2017	2016	2017	2016
Oral PrEP initiations (Q1 2023)[72]	321,622	888,217	165,986	25,617	390,454	25,346	47,542	91,381	440,581	401,083
FP Effort Index[73] (strength of FP program)	49.4	60.8	58.7	52.3	43.9	N/A	47.6	42.2	40.7	51
PrEP ring implementation studies[74]	X	X	X	X				X		X
CAB for PrEP implementation studies[75]	X	X	X	X (planned)	X	X	X	X		X
YGF PrEP Matching Funds[76]	$3m	$5.75m			$3m				$6.5m	$3m
PEPFAR CAB supplies (# people)[77]	Priority waitlist	Starting 2024/25	Starting 2024/25	Starting 2024/25	8k-10k		10k	Starting 2024/25	Priority waitlist	10k-12k
MOSAIC countries	X	X	X	X	X			X	X	X
CAB for PrEP trial experience[78]	X	X	X	X		X	X			X
ECHO trial experience[79]	X	X		X	X					

Figure 22: DPP service delivery assessment criteria and prioritized channels most likely to be utilized by user group

	Service Delivery Channel	Alignment with User Behaviors & Preferences	Cost-Effectiveness	Health System Readiness	Strength of M&E Systems	Scalability	KENYA	SOUTH AFRICA	ZIMBABWE
Public	HIV Clinic						1	1	1
	FP Clinic						1	1	1
	DICE/Population-Specific Site						2	2	2
	Mobile Clinic						2	2	2
	CBD Program						X	X	3
Private	Pharmacist (1st re-supply)						1	2	1
	NGO Model/Social Franchising						2	2	2
	General Practitioner/ Private Provider						1	1	1
	University						X	3	3
	Direct-to-Consumer (D2C)						3	3	3
	Telehealth						2	2	3

High opportunity/ Low risk | **Medium opportunity/ Medium risk** | **Low opportunity/High risk/Not enough info**

**Numbers in country columns correspond to the phase recommended to introduce DPP in that channel. "X" signifies channel will not be prioritized.*

Figure 23: DPP service delivery channels most likely to be utilized by user group

Channels	Women (20-40)	Adolescent Girls (15-19)	FSW	Postpartum women	Women using EC/PEP
Public FP/SRH clinics	X	X	X	X	X
Public HIV clinics	X		X		X
Pharmacies	X			X	X
Social franchises/NGOs	X	X	X		
DICEs/Population-specific sites		X	X		
Mobile clinics	X	X	X		
Private providers	X			X	
Universities	X	X	X	X	X
Telehealth	X	X	X		
Direct-to-consumer	X				
CBD programs for FP	X	X			

3. Key Resources

To access key resources that have been referenced throughout this strategy and for the latest materials on the DPP, please visit: https://www.prepwatch.org/nextgen-prep/dual-prevention-pill/.

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Market Preparation and Introduction Strategy

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