Laying the Groundwork for a Strategic Evaluation Framework (SEF) for HIV Prevention and MPT Product Development
The Initiative for Multipurpose Prevention Technologies (IMPT) advances the development of MPTs to address the interlinked risks of unintended pregnancy and sexually transmitted infections (STIs) including HIV, believing that the availability of desirable methods that deliver an array of prevention combinations will improve the lives of women and their families worldwide. Established in 2009, the IMPT is a collaborative network that has engaged product developers, scientific researchers, healthcare providers, funders and community-based advocates in Africa, China, India, the United States and Western Europe behind this common agenda. Leveraging the multidisciplinary expertise of this diverse network, the IMPT works to advance the science to support the development of MPTs and their successful introduction into target populations with high unmet need.

Multipurpose Prevention Technologies (MPTs) are an innovative class of products that deliver varied combinations of HIV prevention, other STI prevention, and contraception and will improve the lives of women and families worldwide.

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For questions or comments, please contact: IMPT@cami-health.org. The IMPT Secretariat is a project of CAMI Health, an organization dedicated to improving the health of women and girls worldwide based in Folsom, CA, USA. CAMI Health is housed at the Public Health Institute.
Introduction

HIV is one of the greatest public health challenges of today, especially for adolescent girls and young women (AGYW) in Sub Saharan Africa (SSA). AGYW make up 30% of all new infections in SSA, and they seroconvert eight times more often than adolescent males in SSA. Researchers have long recognized the need for better HIV prevention for women, and trials such as CAPRISA 004, TDF2, the Ring Study, and ASPIRE revealed promising efficacy data for HIV prevention. However, despite encouraging product acceptability data, some trial participants, particularly younger women, experienced adherence challenges. The limitations of current HIV prevention options illustrate the need for continued innovation of product development strategies built around real-world contexts of populations most at risk.

Unintended pregnancy and sexual health risks are often of equal or greater concern as HIV. Prevention methods that simultaneously deliver HIV prevention and contraception could leverage women’s need and desire for contraception to facilitate HIV prevention. However, the only comprehensive prevention methods currently on the market, male and female condoms, may be scarce or difficult to negotiate by AGYW. Multipurpose prevention technologies (MPTs) are innovative products in development that aim to address this gap, delivering varied combinations of HIV prevention, other STI prevention, and contraception.

Addressing the multiple unmet sexual and reproductive health (SRH) needs of AGYW requires interweaving their daily realities into the technical challenges of product development. One approach to facilitate this is a Strategic Evaluation Framework (SEF), theorized by Tebbey and Rink. The SEF aims to shape product development programs by marketplace need to create products with high health impact. It is comprised of three key components: the Target Market Profile (TMP), the Strategic Target Profile (STP), and the Target Product Profile (TPP).

The TMP includes information on market needs and factors that will impact the viability of a product. Ideally, the TMP identifies the population at risk and their unmet needs, describes potential drivers of use, provides a competitive assessment of comparable, and indicates the economic cost of the relevant health risk. The STP describes the ideal product by listing optimal and minimal targets for market-based attributes. The TPP is structured as a regulatory licensed commercial product label and sets minimal and optimal clinical targets for a product’s indications and usage. Generalized TPPs for two MPT product types have previously been developed through expert consultations.

We conducted research to support the development of a generalized TMP and STP for ARV-based prevention and MPT products, defining the population at risk as AGYW in SSA with a high HIV and unintended pregnancy burden. We aimed to develop a product-agnostic tool that funders and product developers can use as a starting place to further refine with additional information and assumptions for a given product.
Methods

We collected data by conducting a literature review and key informant discussions, focusing on data on AGYW in five SSA countries with high burdens of HIV and unintended pregnancy: Kenya, Nigeria, South Africa, Uganda, and Zimbabwe. The literature review supported the development of the TMP and highlighted where gaps in research persist. Key informant discussions also informed the TMP and defined critical STP characteristics.

Literature Review Methodology
A comprehensive literature review was conducted between January and April 2016 using the following online databases: PubMed, Academic Search Premier, CINAHL, and Google Scholar. Key search term themes included: HIV prevention/HIV prevention product/sexual and reproductive health; acceptability/preference; market study/research; demand forecast; uptake; and adherence. Article inclusion criteria were: published from 2001-present; data collected in Kenya, Nigeria, South Africa, Uganda, and Zimbabwe; and included female study participants of childbearing age (15-45 years old). We screened the citation lists of selected articles and grey literature for additional articles.

Key Informant Discussion Methodology
We identified key informants within the network of stakeholders that comprises the Initiative for MPTs (IMPT) as well as network members’ recommendations. We selected informants for their knowledge of markets for HIV prevention, contraceptive, and MPT products, and to represent a broad range of perspectives from diverse institutions.

We conducted the key informant discussions from March to May 2016 using qualitative methods in both individual and group settings (i.e., a group of respondents from the same affiliation were brought together in one discussion).

Analysis Methodology
We transcribed key informant discussions verbatim and coded transcripts for key themes, excluding topics unsupported by at least three discussions. End-user data in the selected literature were also coded. Within the TMP, we organized data on the population’s drivers of use around the Socioecological Model.(11)

Results

Twenty-two studies met the literature review inclusion criteria (Appendix A). Most studies consisted of populations in South Africa (n=16) and Zimbabwe (n=9). Kenyan women were represented in five articles and Ugandan women in three, while Nigerian women were represented in one article. Often, data collection occurred alongside a clinical trial for one or more of the following types of pre-exposure prophylaxis products: daily oral tablets (n=4), on-demand (e.g., gel, film, insert) (n=9), long-acting topical (e.g., IVR) (n=4), and ultra-long-acting systemic (e.g., implant, injectable, IUD) (n=2). Facilitators and barriers (potential or actual) to acceptability, adherence, and potential future uptake were reported in all study results. We approached 66 stakeholders and conducted 16 discussions with a total of 32 key informants (48.5% response rate). Key informants represented a range of institutional types, including product development organizations, pharmaceutical companies, clinical research organizations, academic institutions, implementer and other research organizations, and funding agencies.
Target Market Profile (TMP)

The TMP includes the population at risk and their unmet needs, drivers of use, a competitive assessment, and the economic cost of disease. By nature of the available literature (12–14) and expertise of key informants, these results do not include a competitive assessment or economic cost of disease.

Population at Risk and Unmet Needs
AGYW in SSA are a heterogeneous population with complex needs for SRH prevention. Individuals vary by geographic setting, sociocultural context, HIV acquisition risk, health, and marital/relationship status. Age-stratified data were provided when possible to focus on AGYW, but these data were often not available. Appendix B provides demographic summaries for each country that outline considerations for focusing on specific population strata for a product development strategy.

Drivers of Use
Drivers of use at all levels of the socioecological model(11) may be incorporated into a product development and introduction strategy. Most of the literature specified product feature preference and acceptability with little direct information on drivers of use for product uptake. However, from the product acceptability data, we inferred several key drivers.

At the individual level, knowledge about HIV transmission and prevention (15–19) as well as agency to obtain existing prevention methods (1,15,18,20) are critical. Women are also concerned about HIV prevention products affecting their fertility (6,21); moreover, key informants noted that the “value” of HIV prevention is not often high compared to other concerns of women.

Individual-level factors are reinforced from both interpersonal relationships and community norms that value fertility and expect women to have multiple children. (6,21) The literature and key informants emphasized the need for partner support, approval, and acceptability; (22–28) which was frequently associated with increased acceptability of a SRH preventive product. (22–24,26–29) Key informants highlighted a need for increased community engagement and more supportive social norms. Context is also important, they stressed, as such needs may vary in urban versus rural settings.

At the organizational level, advocacy and education may facilitate “gate-keeper” buy-in of products, from policy makers to healthcare workers, as these stakeholders influence product availability, access, and acceptability.(26) The appropriate methods for service delivery must also be determined and may vary by geography. Lastly, at the policy level, criminalization of sex work and mandatory permission of a woman’s guardian or husband to access healthcare impacts AGYW’s ability to access SRH prevention services. (4)

Strategic Target Profile (STP)

While Tebbey and Rink propose STP attribute categories, some are not directly applicable to the focus of development for global health applications (e.g., profitability). We included categories when supported by collected data, otherwise, we refined or replaced these categories. The following ten categories on which to anchor product targets emerged: health impact, market segmentation, value proposition, tolerated toxicity/side effects, acceptability, uptake and adherence, costs, accessibility, and community/market engagement. Except where cited, the following section represents findings from key informants.

Health impact
Demonstration of potential health impact through modelling of realistic scenarios plays a central role in determining cost effectiveness and justification of scale-up. Health impact requires efficacy targets
(listed in a TPP) and effectiveness (i.e., preventive efficacy with anticipated correct and consistent use in a real-world setting among those at highest risk, based on TMP data).

**Market segmentation**
Market segmentation highlights key segments of the market from the TMP to which product development and introduction strategies are tailored for impact. For HIV prevention and MPT development, women’s product preferences and use will vary by age, geography, culture, marital status, etc. Published data to inform market segmentation in this context are limited.

**Value proposition**
The value a product holds for a person with a health intervention need, and why this product may be desirable, includes her perceived importance of the public health risk addressed, the spectrum of potential benefits, and the extent to which the product is advantageous over other products. The value proposition exists alongside daily competing priorities; context must be understood and incorporated into product development strategies to achieve impact. An important part of this balance is that prevention requires appealing to otherwise healthy end-users.

Additionally, efficacy, whether proven, perceived or potential, influences product value for end-users, as cited in articles on clinical trials of vaginal rings, (21,27,30) gels,(28,31,32) and a diaphragm with gel,(23,33) Literature suggests that value also may be additive across indications, noting interest in an HIV prevention product that also served as a contraceptive,(6,33,34) including by women who have difficulty negotiating condom use(33) and by male partners.(6) The value proposition of using a product within a trial setting will also be different from that in the real-world.

**Tolerated toxicity/side effects**
The threshold for side effect tolerance from the end-user perspective is not well understood, though in the prevention context is thought to be low. Side effects, whether proven, perceived (including myths circulating in the community), or potential, were commonly cited as barriers impacting uptake of prevention products.(6,35–37)

**Preferred dosing form features**
Data on end-user preferences for product dosing form features, such as shape, color, and size, must be collected and integrated early into the product development process in tandem with TPP dosage form and product description targets. User experiences include: ease of use/comfort,(29,25,30,6) texture (i.e., of ring/insert),(21,31,38) leakage,(22,38) hygiene concerns,(21,32,38) and size (i.e., of ring/insert). (21)

**Acceptability**
Product acceptability is an important contributor to public health impact, but the causal pathway from stated user product acceptability to product uptake and impact among users is complex. A product and its range of features, benefits, and side effects may be theoretically acceptable to an end-user, but acceptability may change with actual product use. Moreover, product acceptability as a predictor of uptake is difficult to establish and understand using current methodologies in product development and clinical trial contexts.

**Uptake and adherence**
Adherence and uptake are difficult to predict and understand, particularly across diverse populations. Robust biological and psychometric measures of adherence to establish more objective and accurate adherence rates for HIV prevention products and MPTs in trials have not been uniformly established and are themselves still under development. Additionally, the relationship between adherence in a clinical trial versus real-world setting is complex. Reported potential facilitators of uptake and adherence
include reduced duration and/or frequency of clinic visits (21,36) and support from a study counselor (26).

Costs
Product cost tends to be a dominant factor in go/no-go decision making throughout the product development process. Considering the range and complexity of cost determinants across the product development timeline, there is debate over the utility and/or feasibility of emphasizing the importance of cost in the beginning of development.

The most common economic metric used in global health is cost effectiveness. In lower resource settings, cost effective HIV prevention interventions have historically ranged between 5 USD to 18 USD per DALY gained, but cost effectiveness data for HIV prevention and MPT products in development are limited (39). Product developer key informants noted the concept of an “affordable” product as desired by both donors and target markets is challenging.

Accessibility (at all access points)
Product accessibility after its introduction in the market is a complex issue, particularly for multi-indication products that could involve navigating autonomously operating types of health care settings such as family planning and HIV. Given potential patient populations within at-capacity health care systems, accessibility should be considered in product development (e.g., what would make it easier for a provider to add the product to their portfolio?). The socioecological context, including stigma, is also critical to examine when considering accessibility.

Community and market engagement
While not strictly a product attribute, engaging the community (including men and healthcare providers) during the product development process will not only generate demand for the product but will also help to facilitate product access and uptake when introduced. Thus, the extent to which a product development program works to create a market for their product, in collaboration with other stakeholders early in the product development process, is an attribute that should be measured and evaluated.

Having identified the most salient STP characteristics for HIV prevention and MPT products under current and future development, the next steps to complete an STP are to establish optimal and minimal targets for each characteristic, grounded in robust data for each product type.

Discussion
This is a pivotal moment in the HIV prevention and MPT fields as they shift to include market-based assessments early and often to improve the likelihood of developing products with high public health impact. The current clinically-driven paradigm for HIV prevention and MPT product development does not generate the data necessary to complete a TMP and STP; thus, critical research gaps remain.

TMP research gaps
The TMP should be created with a clear focus on the market for which the product is being developed and highlight both facilitators and barriers to use. Most existing data are from clinical trials of specific products, where value drivers and user needs may not be representative of these characteristics once the product is introduced in the market (10). To date, there is only one market research study with publicly available data focusing on end-user preferences for MPTs (8). These differences should be considered when attempting to generalize results.
While the available literature and key informant data suggest common themes to characterize the population with need for HIV prevention and MPT products, many are assumptions based on peripheral data and personal experience. For example, within the key themes, data were not stratified by participant age, setting (e.g. urban versus rural), reported relationship status, or level of education, posing a challenge to market segmentation and strategizing around the unique needs of AGYW in varying circumstances.

Overall, each element of the TMP shapes the optimal type of HIV prevention or MPT product for a given woman at a given time in her life. A rich understanding of context must drive product development strategies to foster product acceptability and adherence during clinical trials and further foster access and uptake after product introduction.

**STP research gaps**

For the STP, insights on market segmentation, value proposition, accessibility, and community and market engagement are the most prominent gaps. Current clinical trial methods and research strategies are not designed to directly capture these elements. However, data systematically collected on tolerated toxicity/side effects, preferred dosing form features, acceptability, and uptake and adherence for specific products can provide indirect guidance and highlight areas for additional product neutral research. Current measures for preference, acceptability, and adherence need to be further distinguished, defined, and analyzed. Standardization and precision around these measures will provide meaningful data to drive product development and introduction strategies.

**Relevant new and ongoing projects**

Despite these research gaps, it is critical to note that the HIV prevention and MPT fields are shifting the paradigm of product development to be inclusive of more holistic research approaches, including market research and a greater focus on end-users' perspectives earlier in the development process. There are numerous projects and studies planned or currently underway that intend to address many of the gaps with a common objective of creating efficacious products that women want and can use. (40–45)

It may not be reasonable to expect all data gaps to be generated by developers and clinical trialists, even as the traditional clinical evaluation paradigm evolves. Stakeholders, such as social scientists, market researchers, and implementers focused on product introduction should collaborate with developers and clinical trialists to leverage diverse expertise. Funders, product developers, and other implementers will need to work together to ensure that support and guidance are sufficient to meet STP targets.

**Conclusion**

A completed SEF will be a useful tool for funding agencies to work with their product developers and other implementing partner grantees to help fill identified research gaps and break from the limitations of the current clinical research paradigm. Once targets are set through the SEF, funding agencies will need to work with their partners to ensure that they have the necessary support and guidance to plan and implement effective strategies to meet those targets. When the characteristics of the population(s) with risk change, developers can revise the framework to ensure a meaningful impact remains possible. An important starting point will be to recognize that some tools and guidance already exist around conducting and incorporating end-user research for product development and introduction. (46–49) Additionally, researchers and product developers may have internal documents similar to a TMP or STP, and for global health research to move more efficiently forward, sharing these data that drive product characteristics is key.
Perhaps the most impactful approach, however, will be to continue to build and strengthen multi-sectorial partnerships that leverage the right kinds of expertise synchronously with the product development and introduction timeline.

References


http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3826169/ pmid: 22267018


### Appendix A. Selected articles on end-user research for HIV prevention and MPT product development.

<table>
<thead>
<tr>
<th>Author / Year</th>
<th>Country</th>
<th>STP Category / Product Type</th>
<th>Study Design / Sample Size</th>
<th>Key Findings</th>
<th>Facilitators / Barriers to Product Uptake</th>
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<tbody>
<tr>
<td>Eisingerich et al. / 2012</td>
<td>Botswana, India, Kenya, Peru, South Africa, Ukraine, Uganda</td>
<td>Daily Oral / TDF/FTC</td>
<td>Quantitative analysis N = 1,790</td>
<td>61% of participants indicated “yes, definitely” and 30% answered “yes, probably” when asked if they were willing to use PrEP. Kenyan FSWs were least likely to say yes when asked about willingness to use PrEP under certain circumstances (i.e., in the presence of side effects, in combination with condom use, if they had to pay for PreP, or if they had to be regularly tested for HIV).</td>
<td>Facilitators NA Barriers • Potential side effects</td>
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<tr>
<td>Corneli et al. / 2015</td>
<td>Kenya, South Africa</td>
<td>Daily Oral / TDF/FTC</td>
<td>Mixed Methods (participants selected in FEM-PrEP clinical trial) N = 312</td>
<td>Over 1/3 of women interviewed (n=31) reported that discouragement from their social networks led to their nonadherence and over half (n=72) said that they believed discouragement from within other participant’s social spheres influenced their nonadherence. Common reasons for nonadherence included: daily regimen of pill taking (54%); the context of the trial (i.e., taking an investigational drug) (47%); forgetfulness (29%); fear of side effects (26%).</td>
<td>Facilitators NA Barriers • Lack of social support • Perceived side effects • Perceived sense of efficacy • Daily regimen • Large pill size</td>
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<tr>
<td>Ware et al. / 2012</td>
<td>Uganda</td>
<td>Daily Oral / TDF/FTC</td>
<td>Qualitative (nested within Phase 3 Partners PrEP study) N = 60</td>
<td>Serodiscordance among couples can be “destabilizing,” however, partner support seemed to reinforce adherence to PrEP use.</td>
<td>Facilitators • Partner support Barriers NA</td>
</tr>
<tr>
<td>Smith et al. / 2008</td>
<td>Kenya</td>
<td>Long-acting topical / IVR</td>
<td>Qualitative N = 40</td>
<td>Overall, respondents had positive feedback about the ideal of a microbicidal IVR. Both female and men participants preferred the idea of an IVR over a vaginal cream or gel. “Covert” IVR insertion was both popular and unpopular. Women liked the idea but were afraid that if their client found out it would prevent receipt of payment. Men felt they had a right to know if a woman had an IVR.</td>
<td>Facilitators • Potential efficacy • Long lasting Barriers • Concerns about size and texture • Concerns about hygiene • Concerns about fertility • Concerns about an IVR affecting client’s pleasure</td>
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<tr>
<td>Study Authors / Year</td>
<td>Country</td>
<td>Study Design</td>
<td>Intervention</td>
<td>Sample Size</td>
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<tr>
<td>van Der Straten et al. / 2012</td>
<td>South Africa, Tanzania</td>
<td>Randomized crossover design; mixed methods N = 157</td>
<td>Women accepted and expressed great interest in an IVR that could prevent HIV and/or other STIs. The majority (86%) of women said partner approval was important, yet over half (59%) also indicated that it was important for an IVR to be used without partner awareness.</td>
<td></td>
<td>Potential efficacy</td>
</tr>
<tr>
<td>Montgomer y et al. / 2012</td>
<td>South Africa, Tanzania</td>
<td>Randomized crossover design; mixed methods N = 157</td>
<td>High adherence (self-reported) in both study groups (n=147; 93%). Of those, 120 (82%) reported no IVR removals. Women who indicated that they had no concerns about ring expulsion, women who never experienced emotional problems with the ring, and those who had unprotected sex during the duration of the study were significantly associated (p&lt;.05) with high adherence.</td>
<td></td>
<td>Ease of use</td>
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<tr>
<td>Nel et al. / 2012</td>
<td>South Africa, Malawi, Kenya, Tanzania</td>
<td>Randomized Clinical Trial; Quantitative N = 265</td>
<td>92% of women had perfect adherence. By week 12, 97% of women reported that the ring was comfortable and that they would be willing to use it if the product was found to be an effective form of prevention.</td>
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<td>Efficacy</td>
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<tr>
<td>van der Straten et al. / 2005</td>
<td>Zimbabwe</td>
<td>Quantitative N = 186</td>
<td>Diaphragms were well received among women who were at risk of HIV and other STIs and consistent use was significantly associated with women who reported never using condoms.</td>
<td></td>
<td>Discreet use</td>
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<tr>
<td>Montgomer y et al. / 2010</td>
<td>South Africa, and Zimbabwe</td>
<td>Randomized control trial; Quantitative N = 5045</td>
<td>71.7% (n=1,583) and 51.9% (n=1138) of the female participants ’strongly liked’ the diaphragm and gel respectively. At the time of the exit survey, 96.6% (n=2,263) said they would recommend the combination to a friend if it was proven effective. Women who reported that their partners had favorable reactions were more likely to consistently use the diaphragm and gel (AOR 1.59, 95% CI: 1.19-2.13).</td>
<td></td>
<td>Positive perception of partner’s reaction</td>
</tr>
<tr>
<td>Montgomer y et al. / 2011</td>
<td>Zimbabwe</td>
<td>Longitudinal cohort study nested within a randomized clinical trial (MIRA)</td>
<td>Attitudes and actions of male partners, both perceived and actual, impacted women’s decisions to use “female-initiated” products such as the diaphragm and vaginal gels. Women who had disclosed and received support from their male partners about</td>
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<td>Partner support</td>
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<td>Study</td>
<td>Country</td>
<td>Methodology</td>
<td>Sample Size</td>
<td>Key Findings</td>
<td>Facilitators</td>
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<tr>
<td>Sahin-Hodoglugil et al. / 2011</td>
<td>South Africa and Zimbabwe</td>
<td>On-demand, intermediate acting / Diaphragm + Vaginal Gel</td>
<td>N = 146</td>
<td>Attributes of the product, the relationship between the participant and her partner, and sexual intercourse impacted participants’ responses about acceptability. Being in the study were more likely to indicate both that they &quot;strongly liked&quot; the gel and be consistent users (AOR 1.80, 95% CI: 1.16-2.80, p&lt; 0.01).</td>
<td>Facilitators: Convenience, Ease of use, Ability to wash, Partner support, Perception of durability, Dual protection</td>
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<tr>
<td>van der Straten et al. / 2008</td>
<td>Zimbabwe</td>
<td>On-demand, intermediate acting / Diaphragm + Vaginal Gel</td>
<td>N = 117</td>
<td>Age (AOR = 1.08, 95% CI: 1.01-1.16), consistent condom usage (AOR = 3.85, 95% CI: 1.54-9.63), and having a partner who supported product usage (AOR = 2.66, 95% CI: 1.1-6.39) were independently associated with consistent product use. While participant feedback indicated high acceptability, it was not independently associated with consistent product usage.</td>
<td>Facilitators: Potential efficacy, Partner support</td>
</tr>
<tr>
<td>Terris-Prestholt et al. / 2013</td>
<td>South Africa</td>
<td>On-demand, intermediate acting / Diaphragm, female condom</td>
<td>N = 1017</td>
<td>Effectiveness of HIV prevention was the most important characteristic of a new prevention method based on participants’ responses. Nearly half (48%) of respondents chose microbicides as their preferred potential method of HIV prevention and 90% of respondents expressed interest in trying a microbicide. Women who have had difficulty getting their partners to use a condom were more interested in the new prevention methods than women who do use condoms.</td>
<td>Facilitators: Potential efficacy, Contraceptive component</td>
</tr>
<tr>
<td>Woodsong et al. / 2014</td>
<td>Malawi and Zimbabwe</td>
<td>On-demand, intermediate acting / Vaginal gel</td>
<td>N = 81</td>
<td>Results indicated acceptability of a vaginal microbicide that would protect against HIV as well as unintended pregnancy. 70% (n=141) of respondents from the HPTN 035A trial indicated interest in MPTs. 64% of women (n=58), 70% male partners (n=28), 76% (n=28) of health professionals, and 79% (n=27) of community stakeholders from the HPTN 035A trial had favorable impressions of MPTs. Among Duets male partners, 28 of 30 male partners indicated support of MPTs.</td>
<td>Facilitators: Ease of use, Dual protection, Woman initiated</td>
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<td>Study</td>
<td>Country</td>
<td>Source</td>
<td>Study Type</td>
<td>Sample Size</td>
<td>Findings</td>
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<tr>
<td>Bentely et al. / 2004</td>
<td>Malawi, Zimbabwe, India, and Thailand</td>
<td>On-demand, intermediate acting / Vaginal gel</td>
<td>Mixed Methods nested within BufferGel study</td>
<td>N = 98</td>
<td>The majority of women from the African field sites (Malawi n=20 (92%) and Zimbabwe n=25 (100%)) indicated that they would use an approved product to prevent HIV when interviewed.</td>
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<tr>
<td>Morrow et al. / 2003</td>
<td>South Africa, United States</td>
<td>On-demand, intermediate acting / Vaginal gel</td>
<td>Mixed Methods nested within a Phase I Clinical Study</td>
<td>N = 63 (32 from SA)</td>
<td>The majority of women (77%) preferred a product that would protect from a range of indicators (HIV, other STIs and contraception). It was also indicated that they would like a product that did not have a contraception component. Safety, ease of use, and impact of sexual pleasure were noted as having the greatest impact on women's acceptance of a microbicide product.</td>
</tr>
<tr>
<td>Moon et al. / 2002</td>
<td>Zimbabwe</td>
<td>On-demand, intermediate acting / Vaginal gel</td>
<td>Qualitative</td>
<td>N = 48</td>
<td>Key informants expressed excitement at the potential of microbicide products although there was concern covert use of microbicides could also cause tension within relationships if the male partner were to find out. Further, as fertility is highly valued in Zimbabwean culture, some informants commented that a microbicide that protected from HIV and other STIs may be more acceptable than one that protected from HIV and contraception.</td>
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<tr>
<td>Ramjee et al. / 2001</td>
<td>South Africa</td>
<td>On-demand, intermediate acting / Vaginal gel</td>
<td>Qualitative</td>
<td>N = 243</td>
<td>77-87% of men interviewed indicated that they would like their partners to use a vaginal microbicide if one became available and 80% indicated that they would want to be informed of their partner's choice to use a vaginal microbicide. When asked if they would be willing to pay for microbicide product, men who were attending university were significantly more likely (75%; p=.019) to say yes than men recruited from STD clinics (54%) or the general population (69%). There was also a significant difference in preference for a microbicide over a condom (82% vs 18%; p=.001)</td>
</tr>
<tr>
<td>Becker et al. / 2004</td>
<td>South Africa</td>
<td>On-demand, intermediate acting / Vaginal gel</td>
<td>Qualitative</td>
<td>N = 204</td>
<td>Providers and policy makers support the idea of microbicides but some expressed concern that microbicides would decrease</td>
</tr>
</tbody>
</table>

**Facilitators:**
- Efficacy
- Ability to use covertly
- Efficacy

**Barriers:**
- Worry that use would increase promiscuity
- Feasibility of covert use
- Hygiene concerns
- Creamy consistency
- Leakage of gel
- Hygiene concerns
- Timing of insertion
- Potential adverse side effects
- Leakage
<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Intervention</th>
<th>Methodology</th>
<th>Sample Size</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>van der Straten et al. / 2014</td>
<td>South Africa</td>
<td>On-demand, intermediate acting / Vaginal gel + oral tablet</td>
<td>Qualitative ancillary study conducted concurrently with randomly selected participants of the VOICE trial N = 102</td>
<td>Few women openly disclosed their nonuse of the trial product they were assigned to and often disclosed that other participants as being noncompliant. Women who participated in the ethnographic interviews (a series of IDIs rather than just one) were more likely to discuss nonadherence. Key themes related to product nonadherence were: ambivalence towards research, preserving a healthy status, and managing social relationships.</td>
<td></td>
</tr>
<tr>
<td>El-Sahn et al. / 2016</td>
<td>Uganda, Nigeria, South Africa</td>
<td>On-demand, intermediate acting; Long-acting topical; Ultra long-acting systemic / Intravaginal film, IVR, implant, injectable</td>
<td>Quantitative N = 1,722</td>
<td>When shown examples and given profiles of four different hypothetical MPTs women were more likely to choose an MPT concept based off their experience and needs. Preference drivers included administration route, ease of use, form, and duration. While 93% reported a preference for an MPT, when asked about their willingness to try the four presented potential products results were as follows: Implant (41%); Injectable (28%); Film (20%); IVR (9%) and none (3%).</td>
<td></td>
</tr>
<tr>
<td>Tolley et al. / 2014</td>
<td>Kenya and Rwanda</td>
<td>Ultra long-acting systemic / Long acting injectable</td>
<td>Mixed Methods N = 223</td>
<td>There was a strong interest in long acting injectables. Among potential end users, high effectiveness was ranked as the most important characteristic of an LAI while providers cited side effects to be the most important characteristic affecting acceptability.</td>
<td></td>
</tr>
</tbody>
</table>

STP: strategic target profile; TDF: tenofovir; FTC: emtricitabine; PrEP: pre-exposure prophylaxis; IVR: intravaginal ring; MPTs: multipurpose prevention technologies
### Appendix B: Demographic summary of target population countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Demographic Summary</th>
</tr>
</thead>
</table>
| Kenya    | - 78,000 new infections; 1.5 million people living with HIV  
- Disease burden is concentrated in urban counties and among the following key populations:  
  - MSM (18.2%), IDUs (12.3%), and FSWs (29.3%)  
  - AWYG three times more likely to have HIV and/or experience sexual violence than their male counterparts  
  - 64.9% AWYG know of at least one formal source of condoms but only 39.6% report ability to obtain condoms  
  - 46.6% AWYG demonstrate knowledge of HIV prevention and rejection of common misconceptions about HIV transmission |
| Nigeria  | - Second largest HIV burden globally  
- 250,000 new infections; 3.5 million PLWH  
- Regional prevalence differences contributed to social norms (e.g. polygamy, genital mutilation, nonsterile bloodletting)  
- 80% of incidence via heterosexual intercourse  
- Modeling predicts 40% of future incidence concentrated among FSWs, MSM, and IDUs  
- Sex workers are eight times more likely to have HIV than the general population  
- 45.5% AWYG know of at least one formal source of condoms but only 12% report ability to obtain  
- 24.2% AWYG demonstrate knowledge of HIV prevention and common misconceptions regarding transmission  
- 35.3% of adults were in favor of condom use as HIV prevention among young people  
- 17.8% of women aged 15-19 years old and 40.2% of women aged 15-24 years old reported to be in age disparate relationships |
| South Africa | - Largest HIV burden globally  
- 380,000 new infections; 7 million PLWH  
- 80% of new infections among AWYG and 175,000 new infections among women aged 25 years and older (2012 data)  
- ~2,500 FSW infected/week  
- Varied prevalence in different provinces – urban informal settlements bearing more of the burden  
- FSW HIV prevalence ranges from 40-88% between regions  
- 10.7% of AWYG have had sex before the age of 15 years old and 33.7% of women aged 15-19 reported having a sex partner who was at least five years older  
- 24.3% AWYG demonstrate knowledge of HIV prevention and transmission |
| Uganda   | - 83,000 new infections; 1.5 million PLWH  
- AWYG account for 4.2% PLWH  
- Highest prevalence in central regions  
- Key populations include: FSWs, fishing communities, uniformed services, and mobile populations  
- Incidence drivers: multiple sex partners, early sexual debut, inconsistent condom use, transactional sex, poverty, and alcohol consumption  
- 6.2% of sexually active AWYG began having sex before the age of 15  
- 35% AWYG demonstrate knowledge of HIV prevention and common misconceptions about transmission |
| Zimbabwe | - 64,000 new infections; 1.4 million PLWH  
- Prevalence “hot spots” concentrated within 11 districts that are: border districts, small scale mining areas, fishing camps, and commercial farming settlements  
- ~50% HIV prevalence among FSW  
- 51% AWYG have had sex before the age of 15  
- 56% of AWYG demonstrate knowledge of HIV prevention and transmission |

PLWH: people living with HIV; MSM: men who have sex with men; IDU: injection drug users; FSW: female sex workers; AWYG: adolescent girls and young women