more of those in the diaphragm groups (n= 78) were comfortable inserting, removing and wearing it. 22% of women in all arms thought the quantity of gel used was too much, though 27% said the diaphragm/gel or gel-only made sex more pleasurable and 23% said it increased sexual frequency. Most (78%) thought the diaphragm was easier to use than male condoms and only 5% preferred the male condom over diaphragm. Over 90% agreed they liked the diaphragm/gel or gel-only because it is woman-controlled and doesn't interrupt sex. 95% agreed they couldn't feel the diaphragm at sex, and 88% couldn't feel the gel. The most common reason for disliking the products was unknown efficacy against HIV/STIs and pregnancy. Overall, only one participant disliked the diaphragm, two participants disliked the gel, and 21% reported disliking condoms. 91% in the diaphragm/gel arms and 100% in the gel-only arm said if proven effective against HIV/STIs they would recommend them to a friend.
Conclusions: The diaphragm and gel were acceptable to a large majority of women. If proven effective against HIV/STIs these products have the potential to be a successful public health intervention.

TUPE0443
Adolescent girls' perspectives on research of female-controlled HIV prevention methods in Kenya

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Background: Few microbicide and cervical barrier effectiveness trials include female participants under 18, a population at particularly high risk of HIV infection. Before these clinical trials involving minors and sensitive topics such as adolescent sexuality can occur, the views of adolescents and the community are needed to optimize adolescent participation in and community acceptance of this research.
Methods: We used 30 semi-structured interviews and 3 focus group discussions (FGDs) with adolescent girls aged 14-17 in Kisumu, Kenya to assess attitudes about current methods of HIV prevention, reactions to a demonstration of microbicide and diaphragm use on a pelvic model, and opinions about microbicide and diaphragm research in adolescent girls.
Results: Content analysis of interviews and FGDs with adolescent girls revealed three key issues. Participants cited condoms and abstinence as options for HIV prevention but felt that neither worked well for adolescent girls. They revealed a fear of novelty and thought that adolescent girls would be scared to be the first group to try a new product. However, the majority of participants felt that both the microbicide and diaphragm would be easy for adolescent girls to use and would be popular methods if they were found to be effective and were available.
Conclusions: Dissatisfaction with existing HIV prevention methods and willingness to try new methods, if found to be effective, support the need for research on female-controlled HIV prevention methods in adolescent girls. Because of adolescent girls' fear of being the first to try an experimental product, safety and/or effectiveness data from adult women may be important in recruiting adolescent girls into clinical trials. We are conducting FGDs with parents and community leaders to discuss the acceptability of this research in adolescent girls, and additional discussions in the community will be needed to determine optimal ways to recruit and enroll adolescent girls into a clinical trial.

TUPE0444
Use of toll like receptor ligands for local innate protection of genital epithelium from sexually transmitted viruses

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Background: The role of TLRs in the process of immune recognition by antigen presenting cells (APCs) is much better understood than the role of TLR expression by epithelial cells. A better understanding of the role of epithelial cells in the process of immune surveillance and host defense is of outstanding importance. We are examining whether treatment of the female genital primary epithelium grown ex-vivo with TLR-ligands/ agonists can induce an innate antiviral state that prevents replication or transmission of sexually transmitted viruses, HSV-2 and HIV-1, through genital mucosa.
Methods: Endometrial and cervical tissues were obtained from women undergoing hysterectomies with their informed consent. The tissues were digested and the epithelial cells were isolated and grown on transwells. Transepithelial electrical resistance (TER) measurements was used to assess the integrity of the confluent monolayer and establishment of tight junctions between polarized epithelial cells. Epithelial monolayers were then treated with different TLR ligands (Poly I:C, Flagellin) for 24h and then infected with HSV-2 or HIV-1. Viral load was detected in the supernatants from apical and basolateral side of the transwells.
Results: Primary epithelial culture model has provided us with useful information regarding the susceptibility of genital epithelium to HSV-2 and HIV-1. Flagellin, a bacterial protein and ligand for TLR-5 was effective in providing 65-80% protection from HSV-2 infection. Poly I:C, a TLR-3 ligand, has been

HIV infection and transmission.
Conclusions: These studies will provide important information [illegible] usefulness of TLR ligands as topical anti-microbials that [illegible] sexually transmitted viruses.

TUPE0445
Discovery, preclinical & clinical development of SPL7013 gel (VivaGel ™), a dendrimer based microbicide for HIV and HSV-2 prevention

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Background: It is well documented that the heterosexual [illegible] HIV is driving the global epidemic. Genital herpes is one of the most [illegible] STIs and is the most common cause of genital ulcers in both developed [illegible] developing regions of the world. A meta-analysis of the risk of HIV [illegible] HSV-2 seropositive persons showed that HSV-2 infection is a [illegible] factor for HIV acquisition. Topical microbicides are products that [illegible] to inhibit the sexual transmission of HIV and other pathogens. [illegible] a target product profile for a microbicide, it is imperative that [illegible] sexual transmission of both HIV and HSV-2.
Methods: Starpharma focuses on the use of dendrimers as drug [illegible] offer a unique platform for exploring chemical diversity on the nanoscale [illegible] production of dendrimer libraries covering a diverse array of micro-environment [illegible] structures can be used in drug discovery and development.
Results: Arising from our antiviral program, early examples of Starpharma [illegible] dendrimers had activity against HIV and HSV-2 which triggered a lead [illegible] optimization process. This work resulted in a series of optimized dendrimer [illegible] microbicides being identified from which SPL7013 emerged as a development [illegible] candidate. Following a range of preclinical studies, Starpharma submitted [illegible] Investigational New Drug application (IND) for SPL7013 Gel (VivaGel™). [illegible] VivaGel™ represented the first time a dendrimer based pharmaceutical [illegible] been submitted to the FDA. A Phase I clinical trial was recently completed [illegible] the clinical development program continues apace focused ultimately on [illegible] the HIV and HSV-2 prevention indications. For HIV prevention, VivaGel™ [illegible] recently granted Fast Track status by FDA. This presentation will describe the [illegible] discovery andpreclinical development that led to the IND filing [illegible] and the clinical data available to date.
Conclusions: VivaGel™ represents an important microbicide candidate [illegible] development for both HIV and HSV-2 prevention.

TUPE0446
High prevalence of abnormal pelvic exam findings among women screened for a vaginal microbicides trial in Malawi

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Background: Abnormal genital findings are common in sexually active [illegible] in sub-Saharan Africa. Because of safety and endpoint concerns, women [illegible] no significant pathology detectable by pelvic examination are preferred for enrollment into vaginal microbicide trials.
Methods: HPTN 035 is a phase II/IIb 4-arm safety and effectiveness study of the microbicides PRO 2000/5 Gel (P) and BufferGel. During the safety phase, HIV-negative women who presented for screening underwent colposcopy examination. Women with deep epithelial disruption or other serious abnormal findings were ineligible until these findings resolved.
Results: In Lilongwe, Malawi, 81 HIV-negative women were screened with a colposcopy. 74 (91%) eventually enrolled. 51 (63%) of women had at least one abnormal finding on their first examination, including 11 (14%) with deep epithelial disruption. 8 (73%) of the 11 women with an epithelial disruption eventually enrolled in the study after STI treatment or spontaneous resolution of findings. Laboratory evaluation revealed 11 (14%) trichomonas, 10 (13%) bacterial vaginosis, 3 (4%) vaginal candidiasis, and no Gc, CT, or syphilis. Women with infections were treated and enrolled when their symptoms resolved.

Abnormal Findings on First Pelvic Exam with Colposcopy	*Prevalence (n=81)*
Petechia/Ecchymosis	31%
Abnormal Vaginal or Cervical Discharge	25%
Erythema	26%
Abrasion	7%
Cervical Motion Tenderness	6%
Ulceration	4%
Laceration	2%
Other Abnormal Finding	6%

[illegible] previously or after STI treat[illegible]

TUPE0447
[illegible] microbicides development programme, Tanzania. Are high risk women who work in bars, guesthouses and similar facilities a suitable study population for clinical trials of vaginal microbicides in Africa?

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[illegible] 1573 women aged 16-54y working in bars, restaurants, hotels, [illegible] as local food-handlers were enrolled, interviewed and examined [illegible] based reproductive health clinics, provided specimens for HIV/ pregnancy testing, and asked to attend for follow-up every three [illegible] positive and negative women were eligible to enter the feasibility [illegible] receive free reproductive health services at any time.
[illegible] baseline prevalence of HIV was 25.5%; pregnancy 9.7%; herpes [illegible] type-2 (HSV-2) infection 74.6%; active syphilis (TPPA+/RPR+) [illegible] bacterial vaginosis 52.6%; gonorrhoea 5.5%; chlamydia 5.9% and [illegible] is 12.3%. HIV prevalence at baseline increased with age, was [illegible] among local food-handlers and women working in traditional bars, [illegible] women and those with fewer sexual partners, and was associated with [illegible] infection and bacterial vaginosis. The incidence of HIV was 3.5 / 100PYs [illegible] 2.4, 5.2). Among 731 HIV sero-negative, non-pregnant women who [illegible] a second visit, subsequent follow-up at 3, 6, 9 months was 83.9%, [illegible] and 72.4% respectively and 78.6% overall. Older women, those who [illegible] moved home or changed their place of work in the last year, and [illegible] working in traditional bars or as local food handlers had the highest re- [illegible] HSV-2 incidence was 18 / 100PYs (95% CI 11.2, 28.9); bacterial [illegible] 44.7 / 100PYs (95% CI 35.7, 55.9); active syphilis 3.4 / 100PYs (95% [illegible] 6.4). The incidence of pregnancy was 44.7 / 100PYs (35.7, 55.9).
Conclusions: These findings suggest that women working in food and [illegible] outlets are likely to be a suitable study population for microbicide [illegible] other HIV prevention trials in Tanzania.

TUPE0448
The effect of one versus two efficacy trials on statistical power, size and costs of phase III programs for microbicides

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Background: The FDA requires one pivotal trial or two trials that demonstrate efficacy for licensure of microbicides, but if two trials are done, each must show efficacy. Developers can conduct one pivotal or two smaller efficacy trials for Phase III programs. We assess the impact of one versus two trials on statistical power, sample size and cost of Phase III programs. Statistical Power = sensitivity to detect efficacy. Low power equals high probability of rejecting truly effective products by chance: 80% power represents 20% chance of rejecting effective products by chance alone. A key observation is that the power of Phase III programs with 2 trials is the product of each trial's power, e.g., 2 trials with 80% power each has programmatic power of 0.64 (=0.8 x 0.8)
Methods: Sample size was calculated for overall Phase III programs to have 90% or 80% power, assuming 50% efficacy, 1:1 randomized placebo-controlled 2-year long trials, 3% HIV incidence, 15% drop-out using Stata. FDA indicated p=0.005 is acceptable for one trial; p<0.001 was calculated for sensitivity analysis. Costs used were US $9,000 per participant.
Results: Required sample size and costs for Phase III programs to have 90% or 80% power are shown below:

Power of Program	One Trial (p<0.005)	One Trial (p<0.005)	One Trial (p<0.005)	Two Trials (p<0.05 each)	Two Trials (p<0.05 each)	Two Trials (p<0.05 each)
	Power	Sample size	Cost (mln)	Power	sample size	Cost (mln)
0.9	0.9	7,995	$72	0.95	10,278	$92
0.8	0.8	6,431	$58	0.89	7,831	$70

Conclusions: To achieve 90% power for microbicide Phase III programs, one pivotal trial at p<0.005 provides savings of 57% in sample size and $41 million versus 2 trials. With p<0.001, one versus two trials provides savings of 27% in size and $24 million. One versus two trials provides significant savings if statistical power for Phase III programs is held constant.

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Background: As the need for populations for Phase III HIV prevention trials grow there is a need to identify multiple sources of potential cohorts. Given the association between HIV and other STDs, STD patients may be suitable for such trials depending on the ability to recruit and retain them in cohorts which have high HIV incidence rates.
Methods: All women aged 16-35 years utilizing the STD Clinic in central Durban between July 2005 and November 2005 were provided information and education on STD, HIV and HIV testing. After individual counseling and HIV testing, HIV negative women were invited to participate in a HIV seroincidence cohort study being conducted in preparation for proposed microbicide and vaccine trials. Following enrolment, study participants attended monthly follow-up visits and had repeat HIV testing quarterly.
Results: The prevalence of HIV infection in the 1259 women screened during this period was 59.3% (95% CI: 56.4-61.9). On average, 21 HIV negative women were accrued each month. A total of 104 women were enrolled. The median age was 22 (IQR 21-24 years). A cohort retention rate of 95.0% per annum was achieved. The women reported 2.2 (SD 1.8) coital acts per fortnight. About 47% reported condom use; a third of them reported 100% condom use. The incidence rate of STIs is 223.7/100 (95% CI: 176.1–271.2) person years. 41 of the 104 women (39.4%) had at least one incident STD during follow-up, whilst 10.6% had more than one incident STD. The HIV incidence rate in this cohort to date is 7.9/100 (95% CI: 0-16.8) person-years.
Conclusions: It is feasible to recruit and retain a cohort of high risk women attending a STD clinic. The high HIV and STD incidence rates in this cohort make them well suited for Phase III microbicide, vaccine or other HIV prevention trials.

TUPE0450
The setting of new or anonymous sexual encounters predicts risky sexual behavior and new sexually transmitted infections among MSM in the multicenter AIDS cohort study (MACS)

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Background: Men who have sex with men (MSM) meet new sexual partners in a variety of settings. We determined the settings in which the greatest proportion of MACS participants met new sexual partners, studied the association of these specific settings with risky sexual behavior and newly acquired sexually transmitted infections (STI), and compared the findings in HIV-positive and HIV-negative men.
Methods: 1683 men (794 HIV-positive, 889 HIV-negative) met new male sexual partner(s) since the previous semiannual visit, 2003-2005. Participants reported whether they met a new partner at one or more of 8 specific types of settings. We assessed predictors of risky sexual behavior (unprotected anal intercourse with >2 or more partners) and STI using multivariate logistic regression overall and separately for HIV+ and HIV- men.
Results: The most common settings for meeting new sexual partners were the internet (34.3%), bars (31.8%), and bathhouses (28.7%). Men were more likely to report having risky anal sex if they met a new partner through the internet (OR 1.91, 95% CI 1.53 - 2.37), in a bathhouse (OR 1.77, 95% CI 1.42-2.21), or in a bar (OR 1.30, 95% CI 1.07 - 1.58), compared to men who did not meet partners in these settings. Men were significantly more likely to report having a new STI if they met a new partner through the internet (OR 1.59, 95% CI 1.13-2.23) or a bathhouse (OR 1.51, 95% CI 1.07 - 2.14). HIV- men avoided unprotected receptive anal sex (URAS) with new partners, whereas HIV+ men engaged in both URAS and unprotected insertive anal sex (UIAS) at significantly higher rates than HIV- men regardless of venue.
Conclusions: The most commonly used settings where MSM in the MACS met new partners were consistently associated with risky sexual behaviors and STI. These settings should be high-priority targets for prevention interventions.