The Initiative for Multipurpose Prevention Technologies (IMPT) was established in 2009 to unite researchers, health care providers, policymakers, advocates, product developers, and donors to advance the development and introduction of products that simultaneously address multiple sexual and reproductive health needs, namely unintended pregnancies, sexually transmitted infections (STIs) including HIV, and other reproductive tract infections. Such products are referred to as Multipurpose Prevention Technologies (MPTs; see below). The IMPT works to: mobilize financial, scientific, and political resources to advance the development of and access to MPTs; build synergy and collaboration among scientific disciplines to expedite product development and implementation; and use a cross-disciplinary advocacy strategy to promote increased support for MPTs. The IMPT Secretariat is housed at the Coalition Advancing Multipurpose Innovations (CAMI), a project of the Public Health Institute, Oakland, CA, USA.

Multipurpose prevention technologies (MPTs) for sexual and reproductive health include vaccines, microbicides and devices (e.g. intravaginal rings, diaphragms) each of which would simultaneously address multiple sexual and reproductive health needs, including prevention of unintended pregnancy; prevention of sexually transmitted infections (STIs), including HIV; and/or prevention of other reproductive tract infections (RTIs), such as bacterial vaginosis or urinary tract infections. Safe and effective MPTs that are also acceptable, affordable, and made widely available would greatly improve health and save resources across the globe.

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An electronic version of this document is available at www.cami-health.org. Other organizations that support the Initiative can post this document on their websites as well. For questions or comments, please contact: cami@cami-health.org.
Executive Summary

Summary of Recommendations and Conclusions

This report summarizes the key recommendations and suggestions from the Product Prioritization Stakeholder Meeting held 26 October 2012. This meeting was part of a process undertaken by the Initiative for Multipurpose Prevention Technologies (IMPT) Scientific Advisory Working Group (SAWG) to catalyze the strategic development of technologies to protect women from unintended pregnancy, HIV and other sexually transmitted infections. The meeting brought together diverse experts to review the SAWG’s preliminary recommendations on product profile, priority candidates, and gaps. This process will also include future vetting by other key stakeholders.

Overall, the meeting participants strongly commended the SAWG’s work, and endorsed its key recommendations and priorities. The experts also provided detailed feedback regarding a number of challenges, risks and strategies to be considered. During panel presentations and lively discussions the group provided a number of constructive suggestions and recommendations, which are summarized below.

Priority Area 1: Active Pharmaceutical Ingredients (APIs)

Experts at the meeting concurred with the SAWG’s prioritization of anti-retroviral-based APIs for HIV prevention, and hormone-based APIs for contraception. They also agreed with the SAWG on addressing the lack of APIs that specifically target other sexually transmitted infections (STIs), a key element needed for MPT development. In addition to these overriding perspectives, the expert group offered the following feedback related to APIs:

• Consistent with the SAWG recommendation, meeting participants endorsed the notion that drug development for MPTs and for topical HIV prevention is overly focused on reverse transcriptase inhibitors (RTIs), especially tenofovir.

• The SAWG had recommended, and the experts agreed, that seeking alternatives to small organic molecules for HIV prevention is a priority. However, most alternatives are at an earlier stage of product development. This is an important gap.

• Overall the group endorsed levonorgestrel as the contraceptive hormone to use in MPTs, as it is well-characterized with a good safety profile. The group emphasized that the investigation of other HC options should continue. (It was acknowledged at the meeting that further research is needed to address outstanding questions around hormonal contraceptive use and HIV acquisition.)
• **Non-hormonal options for contraception** are a clear priority, given their potential for fewer side effects and use in “on demand” products (see below). However, non-hormonal options are still at a very early stage of post-discovery evaluation and are, therefore, of limited availability for development.

• Given the limited options for APIs that prevent other sexually transmitted infections, **identifying potential actives for both bacterial and viral STIs is a priority.**

**Priority Area 2: Formulation and Delivery**

The expert group endorsed the SAWG’s prioritization of a suite of MPT product formats, including sustained release device (e.g., vaginal ring), co-administered injectable, and on-demand type formulations such as films, gels and tablets that can be used at the time of sex. They noted **a number of outstanding issues related to these different technologies**, and underscored the importance of anticipating and identifying ways to resolve them.

• **MPT rings will likely face a number of technical challenges,** including manufacturing that is scalable and cost-effective given the technical complexity of co-formulation as well as limited raw materials and manufacturing expertise.

• Participants at the expert meeting underscored the critical need for data on acceptability and use of rings in key user groups and settings worldwide, including identifying approaches to help women become familiar and comfortable with this technology.

• Even when products are “acceptable” there can be other barriers to use, and women’s reported preferences do not necessarily correspond with their behavior and product use. **Better data are also needed to define uptake and use potential for any MPT product configuration.**

• Despite concerns about adherence, **on-demand products should remain a priority** given infrequent sex, the products’ often discreet nature, the lubricating properties of gels, and generally limited side effects.

• Given that the use of hormonal contraception in on-demand products will likely lead to unacceptable disruptions to the menstrual cycle, cervical barrier methods combined with an anti-HIV or –STI active are a possible near term approach for on-demand MPTs.

Developers should **not assume that bridging studies will be sufficient for regulatory agencies to consider changes in formulation and delivery,** and should refer to specific regulatory guidance.
Priority Area 3: Coordination and Process

• The lack of a **standardized process for go/no-go decisions in R&D**, including **formulations and design issues that affect behavior**, is a critical gap for MPT development.

• Donors and potential industry partners voiced clear support for the SAWG recommendation to **prioritize product leads across a suite of delivery formats**. Donors and developers **should support that lead (or leads)** with sufficient coordinated investment and collaboration to move it forward. Clear product development and access planning, including manufacturing, licensure and ownership arrangements, should be among the criteria that factor into this prioritization.

• **Identifying and investing in back-up leads** is critical so that MPT development overall does not hinge upon one lead.

• A comprehensive review of potential HIV drugs that are “on the shelf” of pharmaceutical and biotechnology companies is a priority, in order to identify **leads** with properties that make them viable candidates for topical formulation and/or systemic prevention.

• Identifying specific properties needed in drugs and other clear contributions that industry can make is key to building an enabling environment for greater partnership and involvement of the private sector. Clearer and closer partnerships can allow the MPT field to capitalize on industry expertise in product development overall and with specific product leads.

• **Adapting and adopting the “line of sight” or “end to end” management approaches from industry** that align user and customer needs with product development could help to manage the complex set of factors related to development and delivery. While the specific market dynamics for MPTs may differ from that of typical pharmaceutical products, the concept can and must be adapted and adopted to build the case and facilitate delivery of these public health commodities.

General Comments

• Echoing the SAWG priorities, the expert group noted that donors and researchers need to continue to **invest in and prioritize good basic science that can inform product development and address key challenges and questions**. A key step would be to identify and invest in specific ways to “de-risk” the process for developers across the field.
• Including young women ages 14-17 in research studies is a key gap that needs to be addressed, and should be a priority for the field. This key user group needs to be included in clinical trials in order to facilitate their eventual access to MPTs.

• Developers and donors should build on and expand efforts to incorporate deliverability and access planning as factors guiding prioritization and investment in MPTs.

• Developers and donors working on MPTs should begin now to explore and identify approaches to working across HIV, STI and family planning programming, given that in many international agencies and national health systems these sectors have separate systems and drivers for forecasting, logistics and supply, cost recovery, and many other key aspects of access and delivery.

• Given that regulatory review for MPTs will be complex and new to many national regulatory agencies, it would be helpful to conduct workshops with key national regulatory authorities to familiarize them with the technical and public health aspects of MPTs.

• Meeting participants recommended the MPT development must balance moving forward those products with the most near term potential with continuing to work toward concepts and products that better meet the product parameters specified in the TPP. Those working on MPTs should “dream big” rather than only settling for working on and refining what is already in the near term pipeline.

* Please note that this meeting report provides an objective summary of an expert meeting of donors and others with MPT relevant technical expertise held in October 2012. This meeting was one element of the process on the way to a final Summary of Findings by the SAWG for this first MPT product prioritization and gap analysis, which is expected to be complete in March 2013.
Introduction and Background

This report summarizes the presentations, discussions and recommendations from the Multipurpose Prevention Technologies Product Prioritization Stakeholder Meeting convened on 26 October 2012. The meeting was organized by the Coalition Advancing Multipurpose Innovations (CAMI), secretariat to the Initiative for Multipurpose Prevention Technologies (IMPT). This meeting was one step in an 18-month long process designed to clarify objectives and lay a firm foundation for the strategic development of technologies designed to simultaneously protect women from unintended pregnancy, HIV and other sexually transmitted infections (STIs). Toward that end, the IMPT convened a Scientific Advisory Working Group (SAWG), comprised of representatives from the major donors supporting research on family planning, reproductive health, and HIV prevention as well as other experts in the field.

The SAWG was charged with three main tasks:

• Defining a general Target Product Profile (TPP) for MPTs;

• Proposing which types of potential MPT candidates should be prioritized in the next five to ten years; and

• Identifying significant gaps in the MPT pipeline that would hamper the advancement of the prioritized candidates.

Through a series of consultations, reviews, and global meetings, the SAWG drafted a set of priority product recommendations and identified key gaps in the pipeline. The objectives of the 26 October meeting were to:

• Obtain an expanded, external, expert review of the SAWG’s draft findings regarding priorities and gaps in the MPT pipeline;

• Comment on and analyze the priorities and gaps from four key perspectives: technical feasibility and associated challenges; regulatory considerations; acceptability, use and potential for uptake; and potential for product delivery to the target populations; and

• Increase knowledge and awareness of the potential and risks associated with MPT development, especially among key donor organizations.

The meeting brought together some 35 diverse experts from pharmaceutical companies, academic institutions, national regulatory authorities, and global drug delivery efforts and a number of countries with greatest unmet need for MPT products. They were charged with critiquing and debating the SAWG draft findings. Panel presentations and lively discussions elicited clear feedback and a number of constructive suggestions and recommendations.
Summary of Findings for Review

Joseph Romano, consultant to CAMI, outlined the results of the SAWG process, first defining and summarizing the evolution of the TPPs for MPTs, and then laying out the MPT Product Priorities and Pipeline Gaps to be debated in the meeting.

MPT Target Product Profiles (TPPs)

Given the wide array of possibilities for combining target indications, mechanisms of action, dosage forms and modes of delivery, the SAWG process defined a TPP for MPTs within a conceptual framework that would:

• Define those candidate product characteristics most likely to have the highest potential public health impact in regions with highest unmet need;

• Establish product development standards to inform “go/no go” decisions; and

• Guide donor investment and sponsor development strategies.

Within this framework the SAWG had organized a consultative process that had generated the following general priorities for MPTs based on drug+drug or drug+device combinations:

• Indications: Combining HIV and pregnancy prevention was identified as the highest combination priority, followed closely by a product that would prevent both HIV and non-HIV STIs. Among these STIs, herpes simplex virus (HSV) and human papillomavirus (HPV) were seen as most important. Although not strictly an STI, bacterial vaginosis (BV) was also recognized as a priority indication. An MPT to prevent pregnancy and STI(s) was recognized as important in specific regions of the world, notably the U.S., India and China.

• Dosage and Delivery Forms: Sustained released technologies were identified as a priority to facilitate product adherence, and topical applications were seen as preferable to oral delivery. Vaginal rings were identified as a delivery form that could potentially balance adherence, reversibility and burden on the health system, and could possibly mitigate side effects associated with oral (systemic) delivery. Pericoital (“on demand”) use was seen as preferable to daily dosing.

• Product Attributes: Among numerous specific product attributes, those identified as priorities included a relatively long shelf-life (ideally 36 months), high storage temperature (40°C), and a presentation that could be discretely stored and used.

Prioritizing the MPT Pipeline

After defining the TPP, the SAWG worked to prioritize the “pipeline” of available products and product leads, and to identify gaps and needs in product types, knowledge, formulation, and
public health potential (see Appendix A and www.cami-health.org/MPTPrioritizations.pdf for
detailed slides). A comprehensive list of MPT products or product components was compiled
and then evaluated according to their development feasibility, and whether they duplicated
other leads within the broader MPT pipeline (e.g., number of each product type with same
mechanism of action, chemical class, dosage form, etc.). After a vetting process by experts
using the collaboratively developed TPP, a short list of compounds, formulations and delivery
types emerged. In addition to the TPP findings, the SAWG then assessed these leads
against other key parameters such as the required development time, the entity developing
the product or lead, ease of use, effect on sex, and so forth.

The SAWG considered the potential MPT pipeline with respect to Active Pharmaceutical
Ingredient (API) and product configurations as outlined below.

**Active Pharmaceutical Ingredient**

- It was concluded that small organic molecule anti-retrovirals are the priority for **HIV prevention**. However, alternative mechanisms of action to reverse transcriptase inhibitors (RTIs), especially tenofovir, are needed as these drugs are also front-line treatment in the MPT target populations with attendant concerns about drug resistance. The SAWG concluded that drugs that have already been approved should be prioritized as MPT components over those at an earlier stage of development since much more is known about these approved drugs and the development and regulatory process will likely be faster. Overall, the SAWG felt that peptides and proteins should not be prioritized at this point.

- The SAWG prioritized **hormonal contraceptives** (HC) for the pregnancy prevention indication of MPTs. While levonorgestrel (LNG) was recommended for inclusion and evaluation in MPT products, its known history and safety profile should not preclude evaluation of other hormones as MPT components. HC may not be appropriate for on-demand products used intermittently due to its potential to disrupt the menstrual cycle (and, thus, timing of ovulation and the risk of conception), and cause intermittent bleeding patterns that may not be acceptable to the user. A key gap is the potential association between specific HC and HIV acquisition and progression, and parallel investment is needed to assess its validity.

- With respect to **drugs specifically targeting sexually transmitted infections**, the SAWG recognized a significant gap of options in this area overall, and recommended development of STI-pathogen-specific drugs as a priority for the MPT, even though such work is at an early stage. Ancillary recommendations were to de-prioritize broadly neutralizing strategies and current anti-HSV drugs, which are limited by rapid selection for resistance.
Product Configurations
The SAWG recommended development of a “suite” of product configurations that would meet different needs and preferences. Such a suite would include sustained release forms (e.g. a vaginal ring), long-acting injectables, and on-demand products that can be used pericoitally. The overall goal would be to have an MPT of each type for each of the prioritized combination indications.

- Currently multiple similar vaginal rings are being developed, and a lead product needs to be identified. Furthermore, since the rings in development are overwhelmingly focused on RTIs for HIV prevention, alternative APIs are needed. Despite the recommended focus on rings as one of the priority dosage forms, the SAWG also recognized that there are insufficient data on acceptability, use and uptake of vaginal rings beyond the North American and European markets. This represents a priority gap.

- With respect to long-acting injectables, the group viewed co-administration of products with separate indications as an acceptable priority, and noted that equal duration of effectiveness will be required for the co-administered products targeting independent indications. Although injectable contraceptive options are currently available, few options are being developed for HIV prevention and the field needs to look at additional ARVs.

- Few, if any, contraceptive or STI prevention options are currently being developed for on-demand products. Adherence is a challenge with any user-controlled method, and there are technical concerns about the safety and effectiveness of intermittent use of ARV or HC in on-demand MPT products. Thus, feasible technical options for on-demand products is a significant gap in the MPT pipeline.

Other Research Priorities
The SAWG indicated a number of priorities for early stage development corresponding with gaps identified in the APIs. These include: APIs for specific STIs; non-ARV based HIV inhibitors; non-hormonal contraceptives; and novel on-demand product configurations. The SAWG had debated whether pursuing products that combine a barrier method with a drug (e.g. a diaphragm with an ARV) should be a priority. One advantage is that such a strategy could potentially fill the gap for non-hormonal on-demand products, but concerns remained about the need for correct and consistent product use to ensure effectiveness.

Coordination and Management
Given multiple actors, the urgency of advancing MPT development, and the realities of resource constraints, the SAWG had made recommendations on processes for moving the field forward. It called for donors and developers to come to consensus on development objectives that allow for identification of appropriate lead candidates. Coordinated investment
and collaborative development, supported by a process of partnered management, will be critical to advance this lead.

**Group Discussion**
The topics, priorities, issues and gaps outlined above were the basis for discussion and debate throughout the meeting and prompted some initial feedback:

- The dapivirine ring trials currently underway could provide proof of concept for HIV prevention with a vaginal ring delivering an NNRTI. Such a proof of concept would be meaningful to MPT development strategies. While any failure of the dapivirine ring would be a clear setback for the HIV prevention and MPT fields, it would be important not to hinge all future ring development on these results. Rather, careful analysis would be needed to separate the active drug from the mechanism of action from the delivery mode, in order to determine appropriate focus for further product development.

- The effects of injectable hormonal contraception on HIV acquisition continues to be debated and analyzed in the global public health arena. At the same time, the MPT field is exploring co-administration of separate long acting injectables for HIV prevention and contraception. Work should continue in both of these crucial areas to generate clear evidence that can inform future research and policy priorities.

- Tenofovir may provide dual protection against HIV and HSV-2, but there is little data on potential HSV-2 resistance to tenofovir. Such information may be required for licensing tenofovir for an HSV-2 indication and is currently a gap in the research portfolio.

**Session 2: Technical Perspectives**
Panelists commented and critiqued the technical aspects of the recommended priorities and gaps, and provided comments drawing on their expertise in reproductive biology, anti-retroviral drugs, formulation and production, manufacturing, and acceptability and use. Their perspectives and the subsequent discussion generally sanctioned the SAWG’s prioritization of ARVs and hormonal contraception. The group also endorsed the concept of developing a suite of different product types, with much of the discussion focusing on vaginal rings.

**Greg Kopf**, University of Kansas Medical Center, commended and supported prioritization of levonorgestrel for use in MPTs. The extensive information available, including a demonstrated safety profile, make it a good option for a hormonal contraceptive. **Non-hormonal options for contraception** are a clear priority, given their potential for fewer side effects and use in “on demand” products (see below). However, non-hormonal options
are still at a very early stage of post-discovery evaluation and are therefore of limited availability for development. If developed further some of these leads may be promising for on-demand products. Hormonal contraceptives will likely have limited utility for on-demand products as intermittent use would likely disrupt the menstrual cycle. Finally, he noted that while many women use and like progestins, irregular bleeding is often cited as a reason for discontinuation.

Randy Tressler, National Institute of Allergy and Infectious Diseases (NIAID), focused his comments on the use of antiretrovirals (especially RTIs), and their compatibility with different dosage forms. He voiced concern about the potential for drug resistance inherent in using the same drugs for prevention and for treatment as well as potential toxicity with long-term use of these drugs for HIV prevention. Given the widespread use of tenofovir in treatment, as patients fail on treatment more resistant virus will emerge. Prevention regimens based on tenofovir will not be able to prevent infection with these resistant viruses. He strongly advocated moving to other ARVs beyond Truvada, though he has similar concerns with other non-nucleoside RTIs. Entry inhibitors may have potential but this particular mechanism of action presents certain challenges: target mutation rate; kinetics of viral interaction; and sufficiency of luminal levels. Developers should consider pairing CCR5 blockers with another ARV given their specificity to block tropic CCR5 virus.

Karl Malcolm from Queen’s University Belfast raised a number of questions and issues related to vaginal rings. He reviewed some specific opportunities and constraints for co-formulating combinations of contraceptive hormones, anti-HIV agents and anti-STI agents in both conventional and alternative ring designs. Different ring configurations and polymer types provide some alternative product options for MPT rings. Particular limitations with each of these approaches was discussed, such as the requirement for sufficient drug release, and various manufacturing and cost issues. A number of combination rings are already being developed for HIV and pregnancy prevention, and Karl reviewed these different approaches. An obvious first approach is to combine a progestogen (such as levonorgestrel or Nesterone – both are being developed in single active contraceptive rings) with a potent HIV antiretroviral, such as dapivirine. While there are known issues with delivering sufficient quantities of peptide and protein drugs from conventional ring designs, he noted that a number of new ring technologies are being investigated for the delivery of biomacromolecules.

Possible manufacturing constraints are a major concern with respect to vaginal rings. Even if it is technically feasible to formulate some combinations in a ring, it may be difficult to make them scalable and cost-effective. Only a limited number of companies produce rings, and few
companies are willing to supply the medical grade raw materials needed to produce them. As work on rings proceeds, parallel efforts are needed to identify, anticipate and look for ways to resolve these issues.

**Lisa Rohan**, Magee Women’s Research Institute, focused her comments on the potential and challenges for “on demand” products such as films, tablets and gels. Such products have many positive attributes – they are relatively easy and inexpensive to formulate and manufacture, and raw materials can be easily obtained in many settings worldwide. The discreet nature of films and tablets, the lubricating properties of gels, and the generally limited side effects could make them attractive to some portion of users. She cautioned that it is not practical to use hormonal contraception in on-demand products because of disruption to the menstrual cycle. Consistent with the SAWG priorities, the research community should continue to search for and develop non-hormonal contraceptive approaches that could be used instead. Further, determining the appropriate dosing regimens for on-demand HIV prevention products could be challenging. In other words, how much time in advance of sexual exposure should the drug be dosed? How long after dosing should be recommended before engaging in sex, or is the product immediately efficacious? How long after dosing does the efficacy effect last? Despite these challenges, on demand products have clear advantages that should be exploited and built on.

**Kate Morrow**, Brown University, outlined approaches to incorporating acceptability and user sensory perceptions and experience of formulations and devices into product design. She advocated for the MPT field to approach product design in a rigorous, rational and scientific manner. She identified the lack of a standardized process to quantify design feature assessments as a gap for MPT development, and urged identifying targets for the user experience to be factored into the TPP. Given the diversity of preferences among women within and between cultures, it may be most feasible to identify an acceptable range for individual parameters that will meet most users needs and preferences rather than specific, fixed parameters.

**Discussion**

- Consistent with the TPP prioritizing devices to facilitate product use and adherence, participants debated and discussed the potential for a 3- or 6-month ring. However it would be critical to determine if the concentrations of released drug in vivo would be sufficient to meet the threshold for efficacy for whatever duration ring is contemplated.

- The microbicide and MPT fields should develop contingency scenarios for priority MPTs. For example, developing rings as delivery devices for MPTs should not hinge solely on the outcome of the current dapivirine ring trials.
• Along with product development, the MPT and related fields need to continue to invest in and prioritize system and model development that can inform product development and address key challenges and questions such as: dose selection, surrogates of efficacy, and relevance of models to human outcomes.

Session 3: Regulatory Perspectives

Martha Brady from the Population Council outlined a number of considerations for regulatory review of MPTs. The regulatory pathway for MPT products will likely be complex given that it will involve more than one indication, complex chemistry, manufacturing and controls (CMC) requirements and challenging demonstrations of efficacy. MPTs may also combine drugs, formulations, or devices that are already approved or that have not yet been approved by a national regulatory authority. The regulatory review processes for such products may be complicated, and may also require working across institutional departments and sections within regulatory agencies. Speakers working in regulatory agencies and international organizations were invited to assess the extent to which any of the prioritized products pose regulatory challenges, and identify optimal mechanisms to engage regulators.

Charu Mullick from the Food and Drug Administration (FDA) noted that as combination, multi-indication products, review of MPTs would include assessing how a product works for each pursued indication, and would involve review by several groups within the agency. While in some instances using an already approved or marketed HIV treatment product may be an advantage, she cautioned that certain issues such as potential for resistance development should be taken into consideration when developing ARVs for prevention. In response to the suggestion that bridging studies may be an approach to address changes in formulations or delivery, she directed sponsors to available FDA guidance. Finally, if a device is altered from its approved version, the center responsible for reviewing devices within the FDA will be involved and would need to consider the extent and nature of these changes. Dr. Mullick noted that the FDA can collaborate with WHO, EMA and other regulatory agencies.

Manjula Lusti-Narasimhan, Department of Reproductive Health and Research, World Health Organization (WHO) outlined relevant WHO processes related to the development of normative guidelines for countries, prequalification, and regulatory review, and guidelines. Developing normative guidelines and recommendations for health interventions is a core function of WHO, and this process would commence once a specific MPT product is further developed. For example, with regard to microbicides, WHO is working toward having normative guidance available for publication soon after to first licensure decision to facilitate rapid implementation of tenofovir gel. WHO prequalification verifies the safety and efficacy of health products already approved by a regulatory agency through teams that review good
laboratory practices (GLP) and good manufacturing practices (GMP). WHO encourages manufacturers to undergo prequalification, and many agencies procuring drugs with public funds require WHO prequalification. Given that MPTs are being developed to meet specific public health needs in developing countries, product R&D should take into account the requirements for WHO prequalification. Recognizing that resource constraints in many developing countries can limit capacity for regulatory review, under Article 58 the European Medicines Agency (EMA) and the WHO can collaborate to give a scientific opinion on a product intended for use outside the European Union. Developing policy guidelines and recommendations for health interventions is a core function of WHO, a process that would commence once a specific MPT product is further developed.

Helen Rees from the Wits Reproductive Health and HIV Institute (WRHI) noted that national regulatory authorities are increasingly considering cooperative agreements with international agencies as a means to supplement in-country technical expertise. Given the potentially complex nature of regulatory review for MPTs, she suggested that opportunities for collaboration be explored early. Dr. Rees also cautioned that regulators may want data from their own populations, and careful attention may be needed to the background characteristics of trial populations with respect to prevalence and incidence of key factors such as HIV and other STIs.

Priscilla Nyambayo of the Medicines Control Authority of Zimbabwe concurred with the previous comments, underscoring that regulatory pathways for MPTs will likely be complex and will require a coordinated approach. She noted that national regulatory authorities generally prefer and sometimes require that products be registered in their country of origin. The MPT field and regulators can and should make use of WHO and other existing platforms for collaboration among regulators. It is timely to make key national regulatory authorities aware of this research through workshops or meetings, although establishing a formal working group seems premature. Finally, the people most in need of MPTs are likely to be young people having spontaneous sex, sometimes with multiple partners. She cautioned that although research on safety, efficacy and resistance is necessary, regulators and policymakers need to also consider a realistic balancing for risks and benefits for individuals and for public health in reviewing new products.

Discussion

• While drug resistance may concern regulators, a public health perspective would emphasize risks and benefits for public health overall, rather than for the individual. It would consider the broader impact of a product measured, for example, in terms of infections averted relative to instances of resistance emergence. The FDA demonstrated
such a public health perspective in the Truvada PrEP hearings, although it is not clear that this is the benchmark or that it would apply more broadly. National and global agencies need to continue to monitor and manage both science and perceptions surrounding resistance.

• There are a number of models for regulatory collaboration that could be built on, including regional efforts focused on harmonization. One example cited is the Kenya Pharmacy and Poisons Board being invited to participate in a recent FDA audit of Partners PrEP, allowing them to engage with the research and the issues early in the process. Fostering such opportunities for substantive collaboration among regulatory authorities could have very positive effects on all stages of regulatory review, including eventual licensure.

Session 4: Acceptability and Uptake

Nomita Chandiok of the Indian Council of Medical Research (ICMR) opened this session, designed to assess how applicable the SAWG identified priorities and gaps are to the MPT needs of the world. Panelists commented on their relevance in different regions and any threats and challenges that may be expected related to acceptability and uptake. In India the priority for the population overall is preventing unintended pregnancy, although prevention of HIV and other STIs are also critical. She generally concurred that the SAWG’s priorities are relevant in India, noting that combined hormonal contraception may be more acceptable as it better controls the menstrual cycle. Developing non-hormonal contraceptives and active pharmaceutical ingredients for STIs are also a priority for India. Though vaginal rings could meet a clear need, there is little data on ring acceptability in India, and some concern that early and frequent pregnancies common to many women in India could lead to slippage and expulsion. She suggested exploring how rings could be redesigned to reduce slippage. Similarly, there is little data on acceptability of long-acting injectables. Following a series of political and legal challenges, the Supreme Court banned contraceptive injectables and they are not included in the method mix in India. On-demand products are highly relevant in India given that many women have infrequent sex, and it may be timely to revisit acceptability and use of barrier methods in India. Finally, an MPT effort is forming in India and will take on greater momentum following an international symposium in December 2012.

Elizabeth Bukusi, Kenya Medical Research Institute, spoke eloquently about the realities faced by a young woman in Kenya to highlight the challenges and opportunities for MPTs in Africa. She noted that despite the notion of a “supermarket approach” to contraception, Depo Provera injections remain the most widely used form of contraception in the region. Health systems are generally unable or unwilling to provide other options, suggesting that it may be difficult to engage those systems in providing new MPTs. Even when products are
“acceptable” there can be other barriers to use, and women’s reported preferences do not necessarily correspond with their behavior and product use. Finally, contraceptive programs in most countries in Africa are dependent on donor funding, which can determine which products are prioritized and available. Long term sustainability, while often discussed, has proven difficult in many settings.

Drawing on her work in South Africa, Audrey Pettifor from the University of North Carolina agreed with the identified priorities and gaps, and focused most of her comments on addressing the needs of young women. In many settings, laws or perceived barriers preclude adolescents from participating in research. Excluding young women from trials may hamper eventual access by limiting how the products are labeled. In addition, the trials cannot generate information on participant perspectives and use from this key user group. Young women are participating in a number of behavioral and structural studies that could inform MPT development and introduction, and the field should engage with and build on these efforts. Devising ways to include young women ages 14-17 in research is a key gap that needs to be addressed and should be a priority for the field.

Allen Wu, Nanjing University, outlined a number of factors in China related to the MPT priorities and gaps. HIV is increasingly being recognized in China, with regional data indicating a dramatic increase in several types of STIs in high-risk groups, and low awareness and use of condoms. This is exacerbated by China’s enormous migrant population, a trend that is expected to continue. In terms of priority MPT indications, the highest priority in China is the prevention of HIV & other STIs, followed by STIs & unintended pregnancy, then HIV & unintended pregnancy. Despite policy emphasis on limiting family size, there is still relatively low use of contraception, with IUDs the most common method. The initial focus of dosage form in China should be: Sustained release products; topical over oral products, and pericoital over daily use products. Given the relatively limited experience with other contraceptive methods, more research is needed on acceptability of different delivery approaches to MPTs.

In reviewing the relevance of the MPT priorities and gaps for the Caribbean, Tina Hylton-Kong of the Jamaican site Caribbean HIV/AIDS Regional Training Network, noted the diversity within the region. Her comments were based primarily on the experience of Jamaica and as such may not reflect the region as a whole. HIV prevention is the top priority, and pregnancy prevention also a priority, though more so in some countries than in others. More research would be needed to determine whether vaginal rings would be acceptable; while there is relatively little experience with rings or diaphragms, women do use vaginal products so insertion may not be a barrier. Currently Depo Provera injections are the most common contraceptive, though implants are becoming more popular because of
convenience. Conspiracy theories about underlying racism driving contraceptive provision are not uncommon, and the MPT field should be aware of this potential challenge. Finally, investigators could build on the existing public health infrastructure in the region to conduct research there.

Kathleen Reape from Watson Pharmaceuticals reflected on how the SAWG findings apply to women in the United States, drawing on the literature as well as her experience working in clinical practice and clinical trials. Prevention priorities vary significantly among different population groups and many women most at risk face challenges of availability, access and acknowledgment of risk. Based on existing contraceptive options, women expect high levels of safety and effectiveness. She sees hormonal contraception as a good option for MPTs, especially levonorgestrel, based on its track record of safety and effectiveness. Overall, women in the US find vaginal rings very acceptable once they overcome initial reluctance, underscoring that programs will need to address these concerns and allow women time to get used to a new product. Injections are also well received, though self-administered injections have failed except among the most highly motivated users. Finally, there is some concern that current products may not be as effective in higher weight women, a key concern given the increasing body mass index among women in the US and elsewhere.

Discussion

• Many participants supported the emphasis on adolescents, and suggested that the MPT field prioritize problem solving and creative strategies to include this key population in trials and other research.

• Results from a number of studies underscore the regional and individual differences in product preferences and acceptability relevant to strategic development of MPTs.

Session 5: Delivery Issues

The TPPs included a number of attributes related to product delivery, including shelf life, storage temperature and cost. Speakers in this session outlined some of the wide range of specific issues related to supply and access for public sector and subsidized products. These include raw materials supply, demand forecasting, purchasing, manufacturing, cost, shipping, distribution, health system integration, procurement, provider training and services, other medical support and overall health management. Panelists in this session were invited to comment on potential issues and challenges associated with delivery of the prioritized MPT products based on experience with other health commodities. With regard to the MPT priority product recommendations, the expert feedback from this section emphasized the need for product prioritization and design to be strongly rooted in the elements of delivery and access, to the same degree as technical feasibility and prospects for regulatory approval.
Mark Rilling from USAID outlined some of the challenges in getting products to low-income countries once they are developed and approved. His comments drew primarily on USAID’s work with contraceptives and condoms. Other donors, including the World Bank, the Global Fund, the UK Department for International Development, and the Governments of the Netherlands and Germany, also play a role in the contraceptive commodities arena and bring their own requirements and practices. These and other donors also work in HIV treatment and prevention. USAID purchases a range of contraceptive products but is generally limited to one or two of each type (pill, IUD, etc.). Products must be approved by a stringent regulatory authority (SRA) or through WHO prequalification. However, regulatory approval is not sufficient for a product to be included in the program, with purchasing decision driven by a number of other factors: acceptability to users and providers, affordability as measured by couple-years of protection; and relatively high demand. While price alone does not drive purchasing decisions, it can exclude products, and a product being “new and exciting” is not enough to justify its purchase. Such a product would need to demonstrate a significant advantage for the user or the health system. Procurement agencies generally like choice in suppliers, as single suppliers leave them vulnerable to price fluctuations and stock outs.

Recognizing that country registration is a growing barrier in some instances, USAID will incentivize producers to apply for and maintain registration in key countries. Overall, significant funding increases for commodity procurement seem unlikely, meaning that MPTs would need to compete against existing products and demonstrate sufficient added value to justify what may be higher costs.

Designing services to deliver MPTs may require integrating some elements of HIV prevention or treatment (for example, testing) with sexual and reproductive health services. Ongoing efforts at such service integration can inform this process. Marketing and branding strategies will need to be developed that effectively and appropriately segments the market and clearly distinguishes any new product. Finally, pricing and marketing will need to reflect the total marketplace, and different cost-recovery and pricing approaches which are often quite complex for public health commodities. Among other considerations will be different models for funding and purchasing commodities and for supporting programs to deliver the products.

Alan Bornbusch also from USAID, continued this review, describing the process and decision factors related to the logistics of getting commodities from a country’s port of entry to the intended user. Such a process relies on supply chains, which tend to be under-resourced and stretched in many low and middle-income countries. Therefore, the burden of adding a new product must be weighed carefully. Many challenges of the supply chain are in the “last mile” of actually reaching users, and community-based distribution that takes products to the...
people has worked well in many settings for contraception. The public sector has had mixed results with establishing and maintaining supply chains, with delivery through social marketing schemes generally more effective. Key players working with supply chains are currently building a menu of supply chain models that do work as a resource to the field. Echoing previous comments, obtaining and maintaining country registration can be time consuming and expensive, and as such present a significant barrier; companies often request help from donors with registration. Finally, several challenges for MPTs may derive from their very nature as multipurpose products. Health systems and donors – even the same donors – often use different methods of forecasting, financing, and cost recovery for HIV and family planning programs. These differences may not be insurmountable, but they are challenging and should be addressed and resolved in advance.

Wayne Shields of the Association of Reproductive Health Professionals (ARHP) highlighted the important role that providers play in championing new products, and underscored that their perspectives are important to factor into developing and designing products. It may be useful to harness providers’ knowledge and experience of contraceptive rings and injectables as a resource in product development as well as anticipating delivery challenges and opportunities. As product development moves forward, it will be important to keep providers engaged so they will understand, recommend and advocate for MPTs.

Discussion

• In industry, pharmaceutical companies use “line of sight” or “end to end” approaches to product development that go well beyond technical development and regulatory approval (see also below). This involves an iterative process using a bi-directional flow of information that continuously seeks to align customer and patient needs with the product development. It is a complex process even when managed by a single entity. It has been particularly problematic in public health product development where the process is discontinuous and involves hand-offs among multiple diverse actors with different expertise, funding streams and mandates. It is incumbent on the MPT field to determine how to incorporate this approach into MPT product development.

• Such line of sight management provides key information for manufacturing, such as forecasting demand and determining an acceptable cost of goods. Pharmaceutical companies build manufacturing capacity in advance and at their investment risk, and it is unclear how to adapt this model given the resource limitations of the MPT and related fields. There is growing interest in local manufacturing for public health commodities, but relatively limited experience in practice. Pursuing this will require a clear business case that such manufacturing can compete on quality, capacity, reliability, price and other key factors.
Session 6: Industry Donor Perspectives

Pharmaceutical and biotechnology companies have been important partners in new prevention technologies for a number of years. Several compounds are currently in trials for HIV prevention, all of which were developed and made available by industry. Such partnerships are key to advancing MPTs and other new technologies for public health, and in this context return on investment would be defined by public health impact. Several representatives from Pharma companies were invited to offer industry perspectives on the TPPs, discuss the commercial potential of MPTs, and suggest mechanisms for potential industry support for MPTs.

Peter Williams, of Janssen Infectious Diseases BVBA, urged the field to develop a vision for where the field can and should go, and to dream big – looking to major innovation and not just what exists now. He cautioned that there is currently much less industrial research and development on ARVs as it is seen as a satisfied market with a large number of safe, effective products. Industry is increasingly relying on agreements with generic manufacturers to provide access to drugs so the MPT field should also explore partnerships with generic manufacturers. Few collaborations between research-based companies and product development partnerships (PDPs) have built optimal processes for ensuring that companies stay involved in product development. Replicating cross-disciplinary teams needed to address the complex processes needed for product delivery has also been difficult in these collaborations. Companies also have tools and processes to allow for objective portfolio prioritization, and there may be opportunities to bring this experience to the MPT field.

Alex Rinehart drew on his work at ViiV Healthcare, a company that combined the HIV portfolios of Pfizer and GSK into a pharma company focused entirely on HIV. He underscored the importance of selecting back-up compounds when identifying a lead compound. The HIV prevention and MPT fields are now “holding their breath” in anticipation of trials results on tenofovir gel and dapivirine ring. The pipeline has limited candidates close behind those leads that could move forward rapidly.

Mark Feinberg from Merck noted that many changes are happening within the HIV field, especially in drug development. He supported the need for strong portfolio management balanced across needs and risks. Such prioritization is critical but difficult, and “killing” a lead early can be a kind of success that allows resources to be directed to other promising leads. He sees opportunities for closer relationships between public and private sectors, for example drawing on innovator pharmaceuticals with generics to meet needs where they are not necessarily commercially viable.
Discussion

• Merging two key issues raised in this session, participants discussed how to ensure that product prioritization is reflected in how licenses are ultimately granted. It would be helpful for the field to align around certain priorities prior to companies granting licenses, thereby possibly avoiding some of the competition resulting from different organizations championing different product leads. When companies grant licenses to PDPs they generally expect that the products will move forward in development, and it is frustrating to see promising leads languish for lack of resources or because the company does not remain closely involved in the product development process. A neutral panel of experts managed through the IMPT could help bring more clarity, alignment and prioritization. This in turn may help draw in companies and donors if they are confident that a compound can move forward.

• Providing greater clarity to companies about what specific properties are needed in drugs, specific ways they can contribute, and what the overall process will look like would help to build an enabling environment for industry collaboration. Development plans should outline the entire process, including design of clinical trials, the regulatory environment, and so forth. This will help companies build greater confidence that drug donations and collaborations will yield meaningful results.

• A priority for the field is a comprehensive review of drug candidates “on the shelf” of pharma companies. By applying the parameters consistent with the requirements of MPT products, it may be possible to identify new leads that are optimal for MPT indications. Several participants from pharma noted that it should be fairly straightforward to inventory drugs in companies’ libraries for promising candidates, although no specific plans were put forward.

• In contrast to the HIV field where numerous actives could potentially be brought forward as MPT components, there are few such leads in the contraceptive field. Those that do exist are left over from when the pharmaceutical industry largely stopped working in the contraceptive space. While this limits the scope and opportunities, they are relatively easy to identify.

• Finally, several participants reflected on the experience with collaborations between industry partners and PDPs. Many such experiences were collaborations in name only. Once the drug was turned over to the PDP the company had little involvement, losing valuable expertise on the specific drug and the development process overall. Going forward, industry interest in MPT is such that they will seek more engaged roles in product development and commercialization.

Session 7: Supporters of Sexual and Reproductive Health Research

In this final session, a number of supporters of sexual and reproductive health research
were invited to comment on the SAWG priorities and gaps, including reflecting on how sufficient the SAWG process has been in informing donors about MPT investment strategies. They were also asked to discuss how complementary and coordinated investments in MPT research and development could be achieved among donors, and explore how to expand the donor base for MPT products.

**Stephen Becker** from the Bill and Melinda Gates Foundation (BMGF) commended the process overall and welcomed the opportunity to continue discussing where best to make investments and how to de-risk the process of product development in this arena. He presented the four components of the product development model used by the Foundation to inform its investments, activities and partnerships. Prior to investment in a product lead the Foundation seeks to establish proof of development feasibility and proof of deliverability using a variety of tools and approaches. These elements are then carried forward in work it supports on clinical development, and delivery and access. Echoing earlier comments on the “end to end” model used in pharma, Dr. Becker underscored that work on deliverability is increasingly informing the Foundation’s investments, drawing on market research, as well as modeling impact and cost-effectiveness. He reiterated that MPT development should not be limited by what exists, and charged leaders in the field to think more broadly and boldly about what would best address both the public health imperatives and needs of women.

**Gina Brown** described how the NIH Office of AIDS Research plays a central role in setting research priorities and facilitating research opportunities and collaborations. She commended the SAWG process in bringing the donors together and laying out a method for doing so, and noted the opportunity to build on the strengths and different mandates of the different donors to build a comprehensive body of research.

**Diana Blithe** works on contraceptive development at the National Institute of Child Health and Human Development (NICHD) at NIH and she noted that, in contrast to today’s discussion about ARVs, pharmaceutical companies have not approached NIH to work on development of new contraceptive products. Given that there is so little new work within the pharmaceutical industry in the area of contraceptive development, NICHD has taken the lead on supporting research on novel methods and on improving existing contraceptive options. The most advanced products involve Nestorone (a new progestin) and developing a long-acting levonorgestrel injectable product. Dr. Blithe suggested that it may be possible to conduct some of the contraceptive clinical work for MPTs through the NICHD contraceptive research network.

**Kirsten Vogelsong**, also of the BMGF, echoed previous positive comments on the process, and confirmed that the foundation is committed to supporting development of MPTs and
intends to issue a call for concepts to inform the development of their strategy. Concepts will need to include details addressing regulatory, intellectual property and access issues as well as scientific and clinical development strategies. Incentivize industry partners in product development (for example, an assay that could be used by different developers). She reiterated her concern about grouping non-HIV STIs together, given that the specific drugs, mechanisms of action and strategies would differ significantly, especially between bacterial and viral STIs. Instead she recommended that the STIs and potential leads be distinguished by target and type. Adolescents could be a key target user group for MPTs in the U.S. as well as internationally, due to the incidence of STIs. The research framework for adolescents in the U.S. varies by state, which is challenging but may also offer some opportunities. While companies generally guard their research strategies closely given their commercial value, the field should call on companies for expertise with product presentation and consumer appeal as well as for active drugs.

**Judy Manning** from USAID noted that their work on contraception focuses on refining existing technologies to improve acceptability and affordability, and developing new methods that fill gaps in the existing FP mix. For example, USAID is supporting efforts to develop a 1-year method to fill the gap for women who want to space their children and currently have no long acting options between 3-months (injectables) and 5 years (implants). She underscored the importance of non-hormonal methods for MPTs, given that side effects deter many women from using HC, and also for on-demand methods that meet the needs of women and girls who have episodic sex.

**Heather Boonstra** from the Guttmacher Institute referred to their study on unmet need for contraception, which showed that, in many settings, even when women have access to contraception they do not use it for several reasons. Guttmacher will now look into this in more depth in select countries to try and understand the specific dynamics of availability, access, acceptability and use. This research could generate new insights to inform MPT development and delivery. Leveraging resources is very appealing to U.S. policymakers, and citing interest, involvement and investment from the private sector as well as other governments such as India and China could attract help support for MPT development.

**Nomita Chandhiok**, ICMR, cited this meeting and the IMPT process overall as very helpful in identifying important ancillary issues like access and regulatory matters in addition to product priorities. The ICMR has set up a task force on MPTs charged with articulating research priorities for India, which could lead to an RFA through which ICMR could support work in India. ICMR welcomes the opportunity to build on its established collaboration with the US government, and welcomes the opportunity to engage with other donors in identifying priorities and streamlining efforts.
Looking Ahead

While the recommendations presented in this report are those deemed most scientifically appropriate at this time, it is the intention of the IMPT SAWG to continue to share these priorities and recommendations with other key stakeholders at a number of upcoming meetings. This iterative process, which will continue through the first half of 2013, will involve a standardized format for eliciting feedback and critique. A range of stakeholders, including product developers, regional experts, socio-behavioral scientists, clinicians, donors and others will be invited to offer their perspectives. The IMPT SAWG also anticipates sharing the recommendations among smaller groups of stakeholders such as manufacturers, and pharmaceutical company officials, as well as with individual experts to help optimize and operationalize the key priorities. As the MPT field continues to advance, it is anticipated that the MPT product priorities will also evolve through an ongoing iterative process. The IMPT aims to produce published MPT product prioritization guidelines by the summer of 2013.

The parameters for MPT products as outlined in the TPP and refined through the ongoing consultative process may not correspond with the product leads that are furthest along in the pipeline. Despite the urgent need for MPTs, the IMPT product prioritization process and the agencies and individuals committed to its success must balance moving forward those products with the most near term potential with continuing to work toward concepts and products that better meet the ideals specified in the TPP. More than one speaker at the meeting challenged scientists, developers and advocates working on MPTs to “dream big” and break new ground, rather than settling on refining what is already in the pipeline.
Acknowledgements

For their considerable contributions to the MPT Product Prioritization activities and this report, its authors wish to thank CAMI staff and members of the Initiative for Multipurpose Prevention Technologies (IMPT), Scientific Agenda Working Group (SAWG), and meeting participants.
### List of Participants

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization/Institution</th>
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<tbody>
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<td>Kate Morrow</td>
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<td>Charu Mullick</td>
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*Members of the IMPT Scientific Agenda Working Group, MPT Product Prioritization Activity
Appendix A

Summary of Joseph Romano's Presentation

Multipurpose Prevention Technologies for Reproductive Health
WASHINGTON, DC 2012
Product Prioritization Stakeholder Meeting

26 October 2012
 Sofitel Washington DC Lafayette Square

Speaker:
Joseph Romano, PhD
NWJ Group, USA
Independent Consultant to CAMI

Identification of Key Attributes, and Prioritization of Product Development
Appendix A

Summary of Joseph Romano’s Presentation (con’t)

Complexity of developing MPTs:

INDICATION
- Pregnancy
- HIV
- HSV
- HPV
- Gonorrhea
- Syphilis
- Chlamydia
- BV
- Candida
- Trichomonas

MECHANISM OF ACTION
- Barrier
- Non-HC
- Anti-Microbial
- Anti-Probiotic
- Anti-Viral
- Anti-Fungal

DOSAGE & ADMINISTRATION
- Topical Peri-coital
- Oral Peri-coital
- Topical Daily
- Oral Daily
- Topical Sustained
- Systemic Sustained

FORMULATION & DELIVERY
- Vaginal gel
- Vaginal film
- Vaginal ring
- Non-IIR device
- Oral pill
- Implant
- Injection

Developing Target Product Profiles (TPPs) for MPTs

Why a TPP?
- To identify key attributes/parameters for MPT products that would lead to the highest potential public health impact (i.e., prioritization)
- To guide donor investment and sponsor development strategies

MPT Initiative TPP Working Group Process:
- Solicited expert review from domestic and international SRH researchers on ideal and minimally acceptable thresholds of product attributes / parameters
- Surveyed US and African providers as to key priority attributes for MPTs:
  - 593 US providers who are members of the Association of Reproductive Health Professionals (U.S.-based)
  - 289 African providers attending the 2011 International Conference on Family Planning in Dakar, Senegal
- Consolidate consensus views
Appendix A

Summary of Joseph Romano's Presentation (con’t)

TPP Input from SRH Researchers

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<thead>
<tr>
<th>Critical Attributes Considered:</th>
<th>Key Attributes of MPTs:</th>
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<tbody>
<tr>
<td>Indications</td>
<td>• Indications:</td>
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<tr>
<td>Efficacy</td>
<td>- HIV &amp; Pregnancy</td>
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<tr>
<td>Route of Administration</td>
<td>- HIV &amp; STI</td>
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<tr>
<td>Side Effects</td>
<td>• HSV, HPV, BV</td>
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<tr>
<td>Reversibility</td>
<td>- STI &amp; Pregnancy</td>
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<tr>
<td>Contra-Indications &amp; precautions</td>
<td>• Dosage Forms:</td>
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<tr>
<td>Product Provision (Rx vs. OTC vs. ?)</td>
<td>- Sustained release</td>
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<tr>
<td>IP Status</td>
<td>- Topical over oral</td>
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<tr>
<td>Time to Market</td>
<td>- On demand over daily</td>
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<td>Product Presentation</td>
<td>• Product Related (e.g.s.):</td>
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<tr>
<td>Shelf Life</td>
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<td></td>
<td>- 36 month shelf life</td>
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<td></td>
<td>- Concealable</td>
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Summary of TPP Priorities of SRH Researchers and Providers

SRH Researchers:

- Priority Indications:
  - Pregnancy + HIV
  - HIV + HSV

- Dosage Forms:
  Major determining factor is PRODUCT ADHERENCE, so highest development priority is Sustained Release

US and African Providers:

- Priority Indications:
  - Pregnancy + HIV
  - Pregnancy + HPV

- Dosage Forms:
  US preference for oral; African preference across several dosage forms, which may help to foster greater acceptance / use

Conclusions from the MPT TPP process:

Although challenging, it is possible to identify general development priorities and product design targets for MPTs

- Useful to funders in terms of investment priorities
- Useful to developers in terms of R&D focus
Appendix A

Summary of Joseph Romano’s Presentation (con’t)

IMPT Scientific Agenda Working Group (SAWG)

<table>
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<tr>
<th>Coordinating Committee</th>
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<tr>
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<td>B. Young Holt, CAMI</td>
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<td>P. Harrison, AVAC</td>
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<th>Donor Representatives</th>
<th>Regional Representatives</th>
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<td>S. Ward, BMGF</td>
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SAWG MPT Pipeline Prioritization: Process

- Assemble comprehensive list of MPT-related products/components
  - 10 MPT IVR
  - 3 On-Demand MPT
  - 2 Barrier MPT
  - 23 HC products
  - 10 Single Indication IVR
  - 12 On-Demand HIV Only
  - 2 Injectable HIV Only
  - 2 Lacto-based Products
  - 31 HIV Entry Inhibitors
  - 11 Enzyme Inhibitors
  - 7 Other HIV Inhibitors
  - 29 non-HC products
- Evaluate for development feasibility, and number per product types (MOA, chemical class, dosage form, etc.)
- Evaluate per general TPP findings
- Evaluate per other criteria
- Access expertise from contraceptive field

Outside the SAWG Scope:
- Study-section type review of specific MPT products or component products and technologies
- Recommendations on funding for specific products or technologies
## Appendix A

### Summary of Joseph Romano’s Presentation (con’t)

#### Priorities for Active Pharma. Ingredients (API)

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<tr>
<th>Priority</th>
<th>Priority Rationale / Identified Gaps</th>
</tr>
</thead>
</table>
| ARV for HIV Prevention Indication | • Small organic molecules  
• Approved drugs over early stage options  
• Lactobacillus-based HIV inhibition for early stage development  
• Deprioritize peptides/proteins  
• GAP: alternatives to reverse transcriptase inhibitors (RTIs), since used in frontline treatment |
| Hormonal Contraceptives for Pregnancy Indication | • Multiple options should be investigated (LNG + others)  
• HC selection should be informed by independent study  
• Deprioritize HC in “on-demand” MPT products due to potential disruption of menstrual cycle (hence, cultural acceptability issues)  
• GAP: potential relationship between specific forms of HC (e.g., injectable DMPA) and increased risk of HIV transmission is not sufficiently understood |
| STI-specific API Development | • Alternatives to broadly neutralizing anti-infectives  
• Deprioritize anti-HSV drugs due to rapid selection of resistance  
• GAP: Lack of viable, pathogen-specific options |

#### Pipeline Priority: Develop a Suite of Products

<table>
<thead>
<tr>
<th>Priority</th>
<th>Priority Rationale / Identified Gaps</th>
</tr>
</thead>
</table>
| Vaginal Rings | • ID single lead candidate for Phase 3 efficacy trials  
• Overly focused on RTIs for HIV; alternatives needed  
• GAP: Insufficient data on acceptability, use, uptake |
| Long Acting Injectables | • Co-administration option is acceptable priority  
• Equity in duration of effect required  
• GAP: Insufficient options in development; additional ARVs needed |
| On-Demand Products | • ID single lead per combination indication for Phase 3 trials  
• Overcome adherence issues  
• Deprioritize HC products, given anticipated effects on menstrual cycle and thus acceptability challenges  
• GAP: Safety of intermittent use of ARVs, other anti-infectives  
• GAP: Limited non-HC and STI prevention options  
• GAP: Social-behavioral science to support all options lacking |
Appendix A

Summary of Joseph Romano’s Presentation (con’t)

Process Priority: Coordination Across Donor Investments, Sponsor Development, and Program Management

1. General consensus on priority products, gaps, and development strategies

2. Coordinated approach to ID single lead products for each priority MPT product type

   Example:

   Pre-Clinical, Phase 1, Phase 2

   Single Lead Phase 3
   MPT Vaginal Ring

3. Pooling of capacity, capability, expertise, and other resources between viable development entities interested in MPT products

   ➢ Needs of the MPT field should supersede individual organizational needs

4. Coordinated MPT development via Target Product Profiles specific to product type, and proactive engagement with Regulatory Authorities

MPT Product Priorities and Gap Analysis: General Summary

<table>
<thead>
<tr>
<th>Early Stage R&amp;D Priorities</th>
<th>“Debated” Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. STI-specific APIs</td>
<td>Barriers + Drug MPT products:</td>
</tr>
<tr>
<td>2. Non-ARV based HIV prevention</td>
<td>➢ Fill gap for an on-demand, non-hormonal contraceptive</td>
</tr>
<tr>
<td>3. Lactobacillus-based products</td>
<td>➢ Concerns over correct and consistent use, and thus effectiveness</td>
</tr>
<tr>
<td>4. Non-hormonal contraceptives</td>
<td>➢ Concerns over safety of intermittent use of anti-infective drugs</td>
</tr>
<tr>
<td>5. Novel on-demand product configurations</td>
<td></td>
</tr>
</tbody>
</table>

Process Priorities

1. Consensus on development objectives across donors and developers
2. ID single leads through common R&D pathways using product type-specific TPPs
3. Coordinated investment and collaborative development
4. Partnered development management
5. Early and proactive engagement of regulatory authorities
Appendix A

Summary of Joseph Romano’s Presentation (con’t)

SAWG MPT Pipeline Prioritization Process: Next Steps

- Formation of SAWG
- Assemble Pipeline Data
- SAWG Team Review, Analysis, Debate, etc.
- General TPP Criteria
- Other Eval. Criteria
- Draft Findings Summarized
- Ext. Review/Comment
- Follow Up Actions
- Finalize Findings & Justifications

Expanded Presentations in early 2013 with Sponsors, Industry, Other Donors & Regional Stakeholders