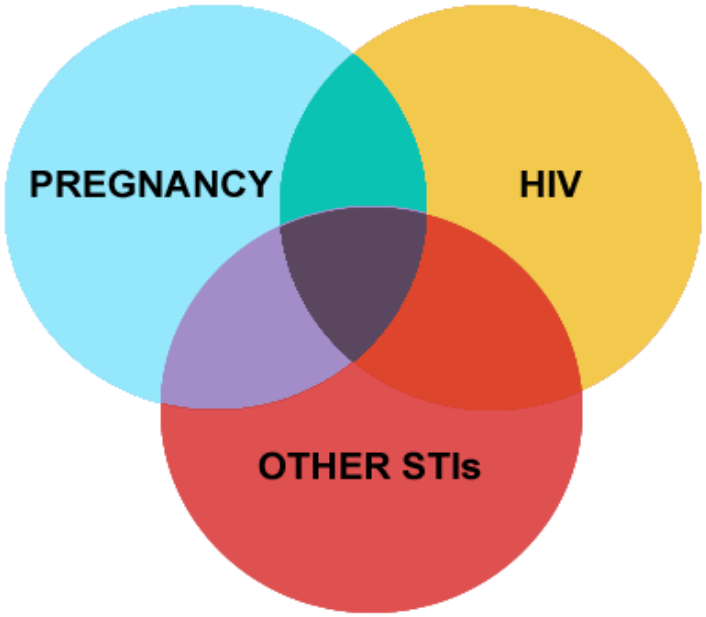

MULTIPURPOSE PREVENTION TECHNOLOGIES FOR REPRODUCTIVE HEALTH

Advancing the Scientific and Product Development Agenda

Report of a "Think Tank"
Washington, DC, USA
5 May 2011

Executive Summary

USAID FROM THE AMERICAN PEOPLE

AVAC Global Advocacy for HIV Prevention

CAMI COALITION ADVANCING MULTIPURPOSE INNOVATIONS

MARY WOHLFORD FOUNDATION

The **Mission** of the Initiative for Multipurpose Prevention Technologies (IMPT) is to raise awareness about and support for the development of multipurpose prevention technologies (MPTs) that can simultaneously address multiple sexual and reproductive health (SRH) needs, specifically unintended pregnancy; sexually transmitted infections (STIs), including HIV; and other reproductive tract infections.

The **Vision** of the IMPT is that those MPTs with highest impact potential are advanced with maximum efficiency and speed, through an integrated development program comprising pre-clinical investigation, translational research, clinical testing, regulatory approval, scale-up, public readiness, and product evaluation. Toward realization of that vision, the IMPT aims to:

- Mobilize financial, scientific, and political resources to support all phases of MPT development
- Motivate synergy and cooperation across scientific disciplines that will help facilitate the sorts of collaborations that can expedite product development and implementation
- Build a cross-sectoral advocacy strategy and cadre of champions for these technologies.

This report was prepared by Anke Hemmerling, University of California San Francisco/Coalition Advancing Multipurpose Innovations (CAMI); Polly Harrison, Senior Advisor, AVAC; Bethany Young Holt, CAMI/Public Health Institute; Judy Manning, US Agency for International Development; Alan Stone, Senior Consultant to CAMI; and Kevin Whaley, Mapp Biopharmaceutical.

It was made possible by the generous support of the American people through the United States Agency for International Development (USAID) under terms of the Cooperative Agreement # GPO-A-00-06-00005-00 and the Mary Wohlford Foundation.

The contents are the responsibility of CAMI/Public Health Institute and do not necessarily reflect the views of USAID or the United States government.

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

Purpose of the "Think Tank"

On May 5, 2011, the US Agency for International Development (USAID), Coalition Advancing Multipurpose Innovations (CAMI), and Global Advocacy for HIV Prevention (AVAC) convened a small group of scientists with expertise in contraception, HIV and STI prevention, vaccines, and devices to discuss and recommend practical strategies for accelerating the development of multipurpose prevention technologies (MPTs) for simultaneous protection against unintended pregnancy, HIV, and other sexually-transmitted infections (STIs).

Meeting Objectives

1. Review some of the ideal characteristics of MPTs for different target populations identified as most likely to benefit from such products.
2. Consider the pipeline of relevant technologies, advise on the steps required for their advancement, and identify further research needs and obstacles.

Define a clear agenda for MPT research and development (R&D) that would provide both the scientific rationale for their accelerated development as well as concrete information for developers, scientists, funders and advocates as to how they could support and further MPT R&D.

Core Definitions

- **Multipurpose prevention technologies** are understood for the purposes of this initiative as strategies that propose at least two health indications (unintended pregnancy; HIV/other STI; RTI). MPTs may include available methodologies; capitalize on emerging technologies or development of new strategies, therapeutic products, vaccines, or devices; and/or drug-delivery systems with potential for enhancing the safety, activity, and potential uptake of these products.
- A **Target Product Profile (TPP)** is both a description of how a proposed candidate product addresses critical attributes, and a proposed framework for its development.

Participant Representation

- Participating USG agencies (besides USAID) included: the FDA Center for Drug Evaluation and Research; and several branches of NIH: the NICHD Contraception and Reproductive Health Branch; the NIAID Division of AIDS and Division of Microbiology and Infectious Diseases; and the National Cancer Institute.
- Participating businesses, foundations, universities and organizations (besides AVAC and CAMI) included: the Association of Reproductive Health Professionals; Dartmouth Medical School; the Bill & Melinda Gates Foundation; Gilead Sciences; the Guttmacher Institute; the Kenya Medical Research Institute; Magee Women's Hospital/University of Pittsburgh; Medsa Ltd.; Mapp Biopharmaceutical; Osel Inc.; the Public Health Institute; and USAID implementing partners CONRAD, FHI360, IPM, PATH, and the Population Council.

Summary of Key Points from the Presentations and Discussions

Introduction

- MPTs are promising in their potential to enable women to simultaneously address multiple reproductive health risks and needs.
- The Initiative for Multipurpose Prevention Technologies (IMPT) is housed at CAMI, which serves as the convener of multidisciplinary meetings and provider of MPT outreach, education, and resource mobilization.

- A framework for MPT development priorities must be devised that weighs candidate products according to avertable risk and highest impact across a range of criteria.
- MPT development cannot be donor-driven for extended periods of time, and must take into account market potential to attract the private sector.

MPT microbicides and devices in the clinical pipeline

A number of promising drugs, dosage forms, devices, and platform technologies already exist as the basis for new MPTs. Issues offering particular challenges to such development are:

- Intravaginal dissolution time of films and tablets
- Tissue concentrations and duration of protection after administration
- Influence of endogenous and exogenous hormones and concurrent vaginal infections on HIV acquisition
- The focus of MPT research and development must be on product candidates that are realistically achievable, and promise high impact and utility in identified target populations.
- Prioritizing is crucial to identify requirements for additional knowledge, mobilize existing expertise, and facilitate productive and coordinated relationships among pertinent research efforts.

Multipurpose vaccines

- The vaccine field has long been using multipurpose vaccines that combine several agents for multiple indications.
- Work on new vaccines is in various stages of research, from basic (e.g., chlamydia, gonorrhea, herpes, syphilis), to advanced (e.g., second-generation HPV vaccines).
- Understanding of mucosal immunity, response measures, and immune tolerance or potentiation remains essential research for all vaccine development.
- Vaccine delivery is evolving, and new techniques are improving the stabilization of existing vaccines and increased shelf life.
- Most multipurpose vaccines were first licensed for a primary indication in a developed country and then expanded to include multiple indications, combinations, and licensure in other countries.
- Vaccines could be a promising option for MPTs since they offer various delivery options, devices and formulations.
- Preclinical candidates for a MPT vaccine could include antivirals against HIV, HPV, or HSV; vaccines against bacterial infections; and contraceptive vaccines.
- In assessing the feasibility of multipurpose vaccines, one needs to consider the needs of end-users, availability of providers and manufacturers, health system infrastructures, and ideal ages for delivery within the spectrum of other vaccines.
- MPT reproductive health vaccines would combine different drugs that have a separate regulatory pathway for each compound. Thus, trial designs would be extremely challenging and require prolonged commitment of time and resources.
- Use of a vaccine platform for delivery of microbicides or combining a future vaccine (e.g., HIV, HPV) with a microbicide to improve overall efficacy merits consideration.
- Rollout of the HPV vaccine in the United States has shown that coverage and user acceptance are low despite an outstanding safety record and level of efficacy.
- The time line for development of combination MPT vaccines for reproductive health is likely to extend further into the future than is the case for other MPT approaches.

MPTs in the preclinical pipeline

- Developing MPTs requires an expansion of the classic pipeline concept to incorporate the three different pipelines for prevention of pregnancy, HIV, and other STIs and RTIs.
- There is now a range of options that merit exploration as MPTs, each in a different stage of development, each with limitations and/or confounding variables that require attention.
- Some microbicide candidates not shown to be effective against HIV but with demonstrated activity against other STIs or RTIs might still merit further exploration as MPT components.
- Single compounds with multiple indications face a complex regulatory pathway. Similarly, a product combining multiple compounds for different indications will be required to demonstrate safety and effectiveness for all drug components and the delivery system itself independently.
- Combining compounds with different pharmacological characteristics is challenging, since they may require different carrier systems to each be released properly.
- Microbicides to prevent HIV transmission are positioned to dominate near–term MPT options, but the MPT pipeline needs to include research beyond anti-HIV microbicides and established contraceptive hormones delivered by vaginal rings.

Rationale for advancing MPTs in the preclinical pipeline

- Preclinical evaluations need to be designed that follow the critical pathway for IND studies set forth by the FDA and other pertinent regulatory authorities.
- Target Product Profiles provide a strategic development process tool based on science, indications, impact potential, and desired product characteristics.
- Establishing “best practices” algorithms for decision-making will help to identify unsuitable product candidates at the earliest possible time point.
- Decisions on product candidates will have to evaluate the relative advantages, novelty, versatility, cost, manufacturing and licensing requirements of new product candidates.
- Even a robust preclinical pipeline will generate only a few candidates suitable for advancement into clinical stages of development, making preclinical research on many compounds essential to the viability and success of the MPT field.
- The development of new STI components suitable for the MPT pipeline could attract new funders whose primary focus is on developed-country markets.

Determining and advancing promising MPT leads

- A robust MPT framework is needed to:
    - Identify target populations across regional, cultural, and socioeconomic backgrounds.
    - Characterize the products best suited to fit their respective needs.
    - Define desired indications, prioritize available drug candidates, and identify research gaps.
- Emerging priority indications for MPTs are pregnancy prevention and HIV prevention. Current stages of development make a combination of antiretrovirals (e.g., tenofovir, dapivirine, or MIV-150) with a contraceptive such as levonorgestrel the most immediately feasible option.
- Gaps in knowledge regarding the effects of hormones on the vaginal mucosa, as well as on differences in female and male metabolism of these combined drugs, will be an obstacle in proceeding with the most feasible option. These gaps must therefore be addressed as basic and translational research to develop parameters for clinical testing of such products.
- Globally, non-HIV STIs are a serious threat to reproductive health and must be an equal driver of the MPT development pipeline. The current focus for MPT vaccines should be on the non-HIV STI indications.

- From a regulatory perspective, the most efficient approach for MPT development is to build on the foundation of already-approved products.
- Advancement of candidates with commercial viability will be critical. Early involvement of private-sector business strategists to evaluate candidates in the MPT pipeline could be very helpful in ensuring eventual product success and sustainability.

Meeting Outcomes and Next Steps

The consensus from the Think Tank was that the development of safe and effective MPTs is clearly feasible, although scientifically challenging. The participants agreed to form two task groups to develop specific TPPs for MPTs, with a focus on the following:

1. Combination products for the prevention of unintended pregnancy, HIV and other STIs
2. Multipurpose vaccines

The task groups will work over the next several months, with the goal of presenting and discussing their respective TPPs at the International MPT Symposium, 3-4 November, 2011 in Washington, DC, USA.

MEETING PARTICIPANTS

Sharon Achilles, *University of Pittsburgh/ University of Pittsburgh/Magee Womens Hospital*

Diana Blithe, *NIH/National Institute for Child Health and Human Development*

Heather Boonstra, *Guttmacher Institute*

Martha Brady, *Population Council*

Elizabeth Bukusi*, Kenya Medical Research Institute*

Ward Cates, *FHI360*

Carolyn Deal, *NIH/NIAID/Division of Microbiology and Infectious Diseases*

Brid Devlin, *International Partnership for Microbicides*

Gustavo Doncel, *CONRAD/Eastern Virginia Medical School*

Cindra Feuer, *AVAC*

Polly Harrison, *AVAC/IMPT **

Monica Kerrigan, *Bill & Melinda Gates Foundation*

Laurel Lagenaur, *Osel Inc.*

Judy Manning, *US Agency for International Development **

Jeff Meer, *Public Health Institute*

Michael Miller, *Gilead Sciences*

Charu Mullick, *Food and Drug Administration/Center for Drug Evaluation and Research*

Jeffrey Roberts, *Food and Drug Administration/Center for Drug Evaluation and Research*

Joe Romano, *Microbicide Trials Network*

Naomi Rutenberg, *Population Council*

John Schiller, *NIH/National Cancer Institute*

Wayne Shields, *Association for Reproductive Health Professionals*

Alan Stone, *MEDSA Ltd./ Senior Consultant to CAMI **

Jim Turpin, *NIH/National Institute of Allergy and Infectious Diseases/Division of AIDS*

Richard Walker, *PATH*

Kevin Whaley, *Mapp Biopharmaceutical **

Charles Wira, *Dartmouth Medical School*

Bethany Young Holt, *CAMI/Public Health Institute/ University of California at Berkeley **

Rapporteur: Anke Hemmerling, *CAMI/ University of California at San Francisco*

Editor and Think Tank Chair: Polly Harrison, *Senior Advisor, AVAC*

** Meeting organizers*