Dear Mr. Wackler,

On behalf of the Coalition Advancing Multipurpose Prevention Technologies (CAMI) and the Initiative for Multipurpose Prevention Technologies (IMPT) we are pleased to submit the attached Request for Information (RFI) entitled **'Building a 21st Century Bioeconomy: The Case for Multipurpose Prevention Technologies'**.

Below are URLs to two documents relevant to this RFI:

Advancing the Scientific and Product Development Agenda. Report of an "MPT Think Tank" (Executive Summary). Washington. DC, USA; May 2011. Hemmerling A., Harrison P., Young Holt B., Manning J., Stone A., Whaley K.
http://www.cami-health.org/documents/050511-MPT-ThinkTank-Executive-Summary.pdf

What Regulatory Guidance Exists for Multipurpose Prevention Technologies (MPTs)? A Review of Key Guidance Documents and Their Applicability to MPTs. Martha Brady and Heeyoung Park. Population Council, 2011
http://www.cami-health.org/documents/What%20Regulatory%20Guidance%20Exists%20for%20MPTs.%20Pop%20Council.pdf

Thank you for the opportunity to submit this RFI. Please contact us if you have any questions.

Sincerely,

Bethany Young Holt, PhD MPH
Executive Director, CAMI | IMPT
Public Health Institute

and

Kevin Whaley, PhD
Executive Advisory Member CAMI | IMPT

Building a 21st Century Bioeconomy: The Case for Multipurpose Prevention Technologies

Introduction:

Every day, more than 1,000 women die from preventable causes related to pregnancy and childbirth. Worldwide, some 75 million unintended pregnancies take place each year and almost half of all pregnancies in the United States are unintended. . Millions are also at high risk of sexually transmitted infections (STIs) and the serious diseases which are often associated with them and take a large economic and social toll on countries. As just one example, the financial burden of dealing with STIs in the United States amounts to about $15 billion annually in direct medical costs alone. Among those burdens is HIV, which remains a serious and challenging global health issue, with 33.3 million people now living with HIV and 2.5 million new cases occurring each year.

Despite the obvious biological, behavioral, and physiological linkages between the risk for unintended pregnancy and STIs, researchers working to prevent pregnancy, HIV, and other STIs have traditionally worked independently in "silos", tackling these interconnected challenges separately. The Initiative for Multipurpose Prevention Technologies (IMPT) has been formed to break open up these silos by providing a steady stream of information and convening researchers, product developers, advocates, and funders to prioritize development of **multipurpose prevention technologies (MPTs)** that can -- simultaneously -- address these reproductive health risks.

The IMPT is driven by the conviction that such lifesaving, potentially cost-effective technologies are scientifically and practically feasible. The types of strategic investments suggested below could accelerate translation of that theoretical feasibility into reality by fostering new collaborations, creating jobs first in academia and small biotechnology companies and then in national and global marketing entities as MPT products are commercialized.

The secretariat for the IMPT is the Coalition Advancing Multipurpose Innovation (CAMI), based at the Public Health Institute. CAMI is pleased, on behalf of the IMPT, to present the ideas below for consideration by the Obama Administration as part of the Office of Science and Technology Policy's Request for Information: *Building a 21st Century Bioeconomy*.

Grand Challenges:

Q1. The grand challenge for multipurpose prevention technologies (MPTs) consists of designing vaccines, contraceptives, microbicides and devices (e.g. intravaginal rings, diaphragms) that address multiple reproductive health needs, including prevention of unintended pregnancy; sexually transmitted infections (STIs), including HIV; and/or prevention of other reproductive tract infections (RTIs), such as bacterial vaginosis or urinary tract infections. While scientifically challenging, development of safe and effective MPTs is technically feasible (Hemmerling et. al., *Report of a 2011 MPT "Think Tank"*). Importantly, MPTs would increase efficiencies for end-users, as well as health care funders and providers, by providing simultaneous protection against multiple health risks, following the continuing trend in pharmaceutical development in general toward development of combination vaccines and therapeutic solutions.

The IMPT proposes that Grand Challenge Prizes for MPTs would be awarded for successfully meeting any number of the following near- term (2-3 years) and longer- term (4-8 years) challenges:

Near-Term Prize 1: ***Determine mucosal tolerance in the genital tract of women.*** Systemic priming followed by mucosal (oral or nasal) boosting is an effective route of the induction of both systemic and mucosal immune responses without the danger of inducing mucosal tolerance. However, this has not been demonstrated so far in the human genital tract.This study would have particular impact on immunization strategies that could prevent HIV and other STIs.

Near-Term Prize 2: ***Develop technology for the robust collection of product adherence data*.** A significant challenge for many HIV/STI prevention studies has been the assessment of end-user adherence to the study product. This prize would address this need and could be some type of electronic or chemical system used to accurately track compliant use of products during the course of clinical trials to allow for appropriate correlation between outcomes and product use.

Near-Term Prize 3: ***Develop at least one robust and predictive pharmacodynamics model for the assessment of MPT product efficacy*.** Typically, very large, expensive Phase 2b or Phase 3 trials are required to establish "proof of concept" – convincing evidence of preventive efficacy. The indications targeted by MPT products desperately and particularly need new, robust and accurate models which can be applied in early stage clinical trials to enhance the predictability of clinical outcomes in later-stage pivotal trials. Therefore, this prize would be awarded to the group or groups that can devise, develop, and validate robust human pharmacodynamics models that can be applied in the early phases of clinical evaluation to assist in product viability assessments and inform investment decisions.

Near-Term Prize 4: ***Develop a prospective, dynamic, and transparent instrument for assessing potential cost-effectiveness.*** The tool should allow developers and funders to iteratively assess the potential cost-effectiveness of MPTs as data become available during clinical evaluation and industrialization.

Longer-Term Prize 5: ***Develop a safe and effective (>70%) multipurpose systemic or mucosal vaccine for reproductive health.*** The vaccine should protect against two or more viral STI pathogens (HIV, HSV, HPV, HBV).

Longer-Term Prize 6: ***Develop a safe and effective (>80%) multipurpose vaginal product that prevents two or more STI/RTI pathogens, or prevents transmission of at least one STI pathogen and is also contraceptive.***

MPT Research and Development:

Q2, Q3 and Q4. The MPT field will not need to create new platform technologies, although it could well to do so, but is more likely to integrate promising, existing platform technologies that will be crucial to successful commercialization of MPTs and to a successful MPT-related bioeconomy. MPT investigators are currently utilizing a broad spectrum of industrialization platforms: chemical synthesis (hormonal contraceptives, antivirals), biotechnology (e.g.,subunit, live, and DNA vaccines, biopharmaceutical microbicides), delivery technology (e.g. intravaginal rings, bacteria, cervical barriers).

Because mucosally-active products for infectious disease indications are a small percentage of antibiotic/antivirals and vaccines, novel and effective MPT-related technology may be relevant to other mucosal infectious disease indications and inflammation. Further, drugs that are restricted to the mucosa would not be drivers of resistance if the virus is not replicating in mucus

Because MPTs are intended for large, cost-sensitive markets, the development and commercialization of these products could have a significant impact on the bioeconomy by broadening market opportunities for other drug products that have been limited so far by cost and scale of production.

Moving MPT Innovations from Lab to Market:

Q5. The primary barrier to MPT innovation is the failure of product developers to create new technologies that simultaneously prevent unintended pregnancy and individual or even multiple STIs. Each of these fields continues to operate autonomously with little coordination or cross-fertilization, despite the obvious synergies.

The Coalition Advancing Multipurpose Innovations (CAMI) guides a global initiative connecting science, industry and education to address the development and introduction of MPTs. The **Initiative for Multipurpose Prevention Technologies (IMPT)** is technology based (i.e., evidence-based science is at the core) and market driven. The IMPT provides a platform for product developers, researchers, donors/sponsors, advocates and clinicians working in sexual and reproductive health to coordinate their efforts and facilitate interdisciplinary research. This interdisciplinary approach provides an opportunity to integrate basic science with behavioral research and market analyses across the entirety of the Critical Path. Such an integrated process could be realistically expected to accelerate time to commercialization, at the same time insuring arrival at MPTs that are safe, effective, acceptable and accessible.

Q6. The **NIAID-AT-SBIR** (the National Institute of Allergy and Infectious Diseases- Advanced Technology-Small Business Innovation Research) program has two milestone-driven phases and appropriate funding (Phase 1 is $600K over two years; Phase 2 is $3M over three years) that could catalyze MPT development if they were a program priority. A study of innovation (Block and Keller 2008) suggests that SBIR-nurtured companies consistently account for a significant fraction of US innovations -- a powerful indication that the SBIR program has become a key force in the innovation economy of the United States. An **MPT-prioritized NIAID-AT-STTR** (Small Business Technology Transfer) program oriented towards academicians could create jobs in universities and non-profits (public health, engineering, clinical trial design and conduct, statistics), and for-profit companies. Equally- funded programs focused on contraceptive development (i.e. a new NICHD-AT-SBIR/STTR) could catalyze the development of new methods for pregnancy prevention.

The current, overarching drug development paradigm is for lead products to be developed by small firms which then partner with large firms for commercialization. Consistent with this paradigm, small innovative firms developing MPTs would be a vehicle for leveraging private-sector funding and thereby having a significant impact on the bioeconomy.
Q7. The MPT field would not require the release of any high-value data by the US Government.

Q8. Approximately two thirds of U.S. innovations involve some kind of **inter-organizational collaboration --** a situation that reflects the more collaborative nature of the innovation process

and the greater role in private sector-innovation by government agencies, federal laboratories, and research universities (Block and Keller 2008). Innovative mechanisms used at USAID and NIH/NIAID (e.g. NIAID's Integrated Preclinical/Clinical Program, U19) that promote a focus on product development and initial clinical trials have been critical to date. Additional programs funded by governments, non-profits and/or for-profits that are oriented around product development (i.e. the safety, efficacy, and industrialization dimensions of the Critical Path) would be undeniably desirable in the future.

Industrialization remains a major risk for the development and commercialization of products (FDA 2004), and is fundamental to the success of the Bioeconomy. Problems in physical design, characterization, manufacturing scale-up and quality control routinely derail or delay development programs and are often rate-limiting for new technologies. MPTs provide a conceptual platform that stimulates innovations for technology platforms, especially manufacturing. Funding rapid, versatile and cost-effective manufacturing systems that are amenable to an iterative process will be crucial for MPT development.

Workforce and MPT Development:

Q9. Professional training programs in a variety of fields should encourage multi- disciplinary collaboration for the creation of MPTs. The natural sciences (chemistry, biology) and bioengineering are, necessarily, intimately involved in creation of new technologies. Equally important is the rollout of new technologies through advocates and program implementers with expertise in international development, public health, sociology and behavioral science. The new field of MPTs will engage all of these fields.

Q10. Community colleges can play a key role in the development and rollout of MPTs, by preparing cadres of pre-professionals trained in the biological, clinical, social and implementation sciences.

Q11. The private sector must play a key role in the conceptualization, creation, testing, and rollout of new MPTs. The ultimate goal of the field is to produce one or more commercially viable technologies that can be disseminated globally by commercial interests. While the potential commercial benefit for such a universal set of products is enormous, the financial and regulatory barriers to creating and testing them will drive the private sector to seek opportunities for collaboration and partnerships.

Q12. While some MPTs are advancing through human studies, others remain purely theoretical or on the drawing board. That said, there remains ample opportunity for the conception of new technologies that fall within existing paradigms (barrier methods) as well as more advanced technologies (vaccines and injectables). Government, industry and academia can separately incentivize research in this area.

Reducing Regulatory Barriers for MPTs and the Bioeconomy:

Q13. If the IMPT is to deliver on its promise, scientific creativity and effort must focus on improving the product development process itself, with the explicit goal of robust development pathways that are efficient and predictable and result in products that are safe, effective, and accessible (FDA, 2004). The IMPT must modernize the critical development path that leads from scientific discovery to end users.

A new product development toolkit — containing powerful new scientific and technical methods such as animal or computer-based predictive models, biomarkers for safety and effectiveness, and new clinical evaluation techniques — is urgently needed to improve predictability and efficiency along the critical path from laboratory concept to commercial product.

The development of MPTs faces similar challenges as other global health initiatives (Bollyky 2011), i.e. two substantial bottlenecks threaten the IMPT's capacity to commercialize products. First, there is not enough clinical research and regulatory capacity in many settings to support the clinical trials that need to occur there in order to complete the development of these products. This lack of regulatory and clinical trial capacity can undermine the safety of subjects and the validity of clinical data. Second, even with expected attrition in the pipeline, current levels of financing are insufficient to support the clinical development of these products under current cost assumptions. Addressing these related challenges will require not only identifying new sources of funding for large-scale clinical trials and capacity building—but also devoting more attention to how these trials and their regulatory pathways can be improved to reduce unnecessary costs, delays, and risks to trial subjects.

Q14 and Q15. The IMPT recommends a two-pronged strategy to bring the costs, risks, and finances for clinical trials for MPTs into a more sustainable balance.

First, establish regional mechanisms for the regulation and ethical review of clinical trials. Moving to a single, integrated process by which clinical trials occurring in multiple countries and sites are approved and overseen would improve the coordination and pool the capacity of ethics committees and national regulatory authorities (NRAs) involved, reduce regulatory inconsistencies and overlap, and provide a more attractive platform for external assistance and donor support. In doing so, regional cooperation would offer the opportunity to improve regulatory capacity and reduce clinical trials costs at fairly low expense to donors and local governments.

Second, better/faster/less expensive clinical trials are needed. Achieving that objective will require a focus on the key parameters and objectives of the trial, evidence-driven approaches, and early engagement among trial sponsors, investigators, and NRAs. Strategies may include:

- *Adaptive study designs for licensure; more support for policy research in phase IV studies.* Focusing pivotal trials on the research necessary to support licensure would reduce costs, expedite product registration, and lower site and investigator demands. For this approach to succeed, however, donors must increase funding for the phase IV *policy and epidemiological studies.
- *Early investigator input and independent advisory committees*. Local investigator and independent stakeholder input should be solicited early in study and protocol design to help spot potential problems and help keep studies simple, feasible, and focused.
- *Pressure-testing protocols.* "Pressure test" protocols and screening criteria by performing them with potential subjects and study products prior to enrollment. This approach improves the efficiency of trial design, reduces the number of subsequent protocol amendments, and ensures recruitment of appropriate subjects into clinical trials.

A New Model for Product Development Partnerships:

Q16. The IMPT seeks to create an environment conducive to self-organizing, decentralized product development partnerships. Existing NIH funding mechanisms that support this integrated approach (e.g. U19s, R21/R33, R43/R44) are desirable for MPTs.

Q17. MPTs represent a uniquely high-impact opportunity or pre-competitive collaboration in life science research and development. This work can and should be informed by successes achieved in the development of many multiple-indication technologies and medicines, including vaccines.

Conclusion:

The IMPT thanks the Administration for offering this opportunity to provide a response to the Office of Science and Technology Policy's Request for Information. We believe that MPTs offer a strong case for a lifesaving technology with the potential for direct impact on the lives of half of the planet's population, as well as a chance for the Administration to demonstrate a commitment to game-changing innovation. The MPT field is poised to become one of the great technology success stories of the 21st century. With a small strategic investment now, the Obama Administration can assure its own place in the history of that dramatic moment, while creating economic and job opportunities through the fields of biotechnology, engineering, manufacturing, international development, and marketing.

References:

Block F and Keller MR. Where do innovations come from? Transformations in the U.S. National Innovation System, 1970-2006. The Information Technology and Innovation Foundation (2008).

Bollyky T (chair). Safer, Faster, Cheaper**:** Improving Clinical Trials and Regulatory Pathways to Fight Neglected Diseases. Report of the Center for Global Development's Working Group on Clinical Trials and Regulatory Pathways. (2011).

FDA. Challenge and Opportunity on the Critical Path to New Medical Products. (2004).

Hemmerling A., Harrison P., Young Holt B., Manning J., Stone A., Whaley K. Advancing the Scientific and Product Development Agenda. Report of an "MPT Think Tank". Washington. DC, USA. (2011).