

Global Health Research at USAID: A Unique and Critical Role

“With its experience in the developing world, USAID does and should play a valuable role in facilitating international clinical trials, consolidating markets, and finding new opportunities to speed the discovery, development, and delivery of products to improve the lives of those in the developing world.”

Congressional response to 2005 USAID report on health-related research and development (from House FY 2006 Foreign Operations Appropriations Committee Report).

For three decades, global health research at the US Agency for International Development (USAID) has supported the development and introduction of affordable health products, as well as policies and practices appropriate for addressing diseases and health issues in developing countries. With a field presence in over 70 countries, USAID leverages its expertise and broad geographical reach to uniquely support and guide such activities. USAID’s on-the-ground expertise in the countries where disease poses such a heavy health burden has established it as one of the most well-positioned agencies in the federal government to conduct the research necessary to ensure that the best available health tools are ultimately used effectively on the ground.

Within the US government, USAID occupies a distinct niche, providing skills and leadership in areas that often fall outside the scope of other US government agencies. While agencies such as the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) perform basic research that plays a critical role in product development, this early-stage research is only one component of the full spectrum of research and development needed to assure that appropriate, affordable, and effective products reach those who need them most.

Basic science alone may suffice for products that have potentially significant commercial markets, because private industry has an incentive to conduct the remaining research to develop, test, and introduce products. However, for products designed specifically for the developing world, private industry is unlikely to invest in these efforts. In these cases, USAID is often the federal agency best suited to support the efforts needed to ensure that basic research breakthroughs are translated into concrete health gains in the developing world. USAID funds are used to apply basic science to health interventions, successfully introduce them to the communities where they are needed, and then rigorously test those interventions for safety and effectiveness.

Success Stories & What is Possible

USAID’s success in applying research and development to disease interventions in the developing world is demonstrated through its proven successes and promising efforts. While these examples represent only a fraction of the research and development work conducted by USAID, they illustrate the distinct potential and impact that USAID has on improving global health.

HIV/AIDS

USAID is deeply engaged in the worldwide fight against HIV/AIDS and the agency's efforts include significant support for at least two critical areas of research: research to develop safe, effective, and acceptable *microbicides* to prevent HIV infections among women, with particular attention to cost and product characteristics for use in developing countries; and research to develop an *AIDS vaccine* intended specifically for use in the developing world.

Microbicides

In addition to supporting clinical trials to develop microbicides, a women-initiated product to prevent HIV transmission, USAID also funds critically important initiatives that support the needs and engagement of the communities participating in the trials. For example, while there is now global consensus that those who are participating in HIV prevention trials should be ensured access to high-quality HIV care, carrying out this responsibility in under-resourced areas in which these trials take place remains a major challenge. In June 2008, USAID funding supported an international consultation to assess how trials had coped with this challenge to date and identify potentially more effective and efficient strategies for the future. The outcome was a concrete proposal to establish a public-private partnership through which publicly funded research networks conducting HIV prevention trials could pay into a trust fund. The fund would be used to provide a uniform HIV-specific care and treatment package for trial participants. Working with the largest providers of HIV care in South Africa, the proposal will be presented to donors, investigators, and trial networks to help provide a concrete mechanism to care for sero-convertors in these trials in the future.

Support from USAID also enabled the development and launch of a "Community of Practice" (CoP) program to facilitate information exchange and skills development among community liaison officers, social scientists, and others involved in site preparation and community involvement at clinical trial sites. The CoP brings together 45 participants spanning 14 countries, 9 different networks/sponsors, and 17 individual trial sites to share strategies and learn from each other to enhance their job performance. Monthly conference calls and tele-briefings provide a forum to discuss practical themes, such as developing terms of reference for Community Advisory Boards, discussing strategies for managing rumors around blood collection, and using participatory techniques to identify community leaders. Information is also made available through a web-based clearinghouse of articles relevant to community and stakeholder engagement. Members can post questions or comments, review standard operating procedures from sister sites, and share resources. Together, the group works to not just talk about the need for greater community involvement and outreach to stakeholders at trial sites, but to actually do the work to make community engagement a reality.

HIV/AIDS Vaccine¹

As an agency committed to international development and a key partner in the expansion of care and treatment to ease the grip of the pandemic, USAID brings valuable expertise and resources

¹ Please note: language on USAID's HIV/AIDS vaccine work is from the USAID website at http://www.usaid.gov/our_work/global_health/aids/TechAreas/research/vaccinefactsheet.html

to the goal of developing a globally relevant HIV vaccine. USAID has in-house expertise in clinical trial design and conduct, immunology, virology, product development, pharmaceutical regulatory affairs, ethics, community engagement, and gender issues. Partnering this expertise with USAID's broad international partnerships in HIV prevention, care, and treatment is fundamental to the eventual success of HIV vaccine discovery and distribution.

Since 2001, USAID has funded efforts to accelerate the development and clinical testing of HIV vaccine candidates. This support is an important part of US government efforts to address the pandemic from multiple directions. Under a five-year cooperative agreement initiated in 2006, USAID is supporting private partners in efforts to strengthen clinical trial capacity in developing countries, advance the development and testing of novel vaccine candidates, enrich the pipeline of next-generation HIV vaccine candidates, and analyze policy and future access-related issues in the HIV vaccine field.

Through its key partnership with outside organizations, USAID engages in HIV vaccine research and development and related activities. As promising vaccine candidates are identified, USAID support its partners' efforts to assess how the availability of an HIV vaccine might contribute to changing risk behavior, and how these effects can be countered. USAID is planning for the introduction of HIV vaccines in developing-country settings. These activities will eventually include engaging host-country governments to register new products, managing supply chain and logistics of vaccine delivery, developing protocols, and training health care workers through partnerships that pre-exist in current USAID networks.

Malaria

Malaria Drugs

Over the past several years, USAID has significantly expanded its support for global efforts to control malaria. Through the use of a combination of interventions, these efforts have already achieved a remarkable degree of success. Anti-malarial medicines have played a prominent role in this success. Unfortunately, the malaria parasite is extraordinarily adaptable, and historically has shown an ability to rapidly develop resistance to first-line medicines. Already, there are indications that some strains of the parasite might be developing resistance to the most effective drugs available. USAID recognizes this threat, and that securing and expanding its advances in malaria control will require the development of new interventions, including medicines. For this reason, USAID has taken a lead role in supporting efforts to develop new medicines for malaria. For example, in January 2009, USAID supported the launch of Coartem Dispersible, a new anti-malarial medicine designed especially for children—the first of its kind to come out of any product development partnership pipeline. This medicine has been clinically proven to be effective in curing malaria in children, and is the first pediatric malaria cure that is dispersible, sweet-tasting, and which has stringent regulatory approval.

Malaria Vaccine

Over several decades, USAID has been one of the most active US agencies in the development of malaria vaccines. Responding to recent advances in understanding of the malaria parasite and in vaccine development, USAID is focused on cultivating new technologies needed to further advance the field. In particular, USAID has expertise in malaria vaccine preclinical development

and clinical evaluation that is second to none. The agency's work in this area includes performing the initial preclinical research that led directly to the development of RTS,S, the world's most clinically advanced malaria vaccine. USAID's flexible funding mechanisms allow it to support the evaluation and testing of investigational vaccines that other agencies are unable to fund—a comparative advantage among US agencies active in this area. Its catalytic role includes the support of new methods to evaluate these technologies and the promotion of shared access among its partners to those cross-cutting tools that show promise.

USAID's research and development strategy is also unique in that it supports activities aimed at accelerating the introduction of the malaria vaccine into endemic countries. Support from USAID has helped to enable the development of a decision-making tool called the Malaria Vaccine Decision Making Framework (DMF). The DMF identifies—in advance—what information a country will need to make a decision on malaria vaccine introduction. This novel tool will reduce the lengthy gap between having a vaccine licensed and having it used on the ground.

Tuberculosis (TB)

TB Drugs

USAID research and development support has played a key role in the global effort to fight TB, filling a critical gap between research and development, and access to the products that are ultimately licensed. USAID plays an important role in the introduction of new products in the field through its leadership of the Stop TB Partnership Retooling Taskforce. In addition, USAID support for large-scale drug registration trials has built research capacity in developing countries most affected by TB. Specifically, USAID support was a central factor in enabling two promising TB drug candidates—moxifloxacin and PA-824—to enter clinical trials. If able to fully fund its renewal pledge of \$40 million over the next five years, USAID funding will allow for continued development of these two candidates, as well as clinical testing for two additional late-stage projects.

TB Vaccine

Given its unique strengths in global health research and development, USAID could also make significant contributions to global efforts to develop a new vaccine to prevent TB. The existing TB vaccine, BCG, was invented almost 90 years ago and has limited efficacy. A new vaccine will significantly advance global efforts to fight this deadly disease, and USAID support and expertise can play a critical role in accelerating its development and availability. Eight potential TB vaccine candidates are entering the clinical testing phase, yet very little capacity exists to conduct registration-quality clinical trials for TB in developing countries where they must be carried out. When these trials begin, USAID could play a central role in supporting field trials in partnership with several organizations.

Neglected Tropical Diseases

Neglected tropical diseases (NTDs) are a group of thirteen major parasitic and bacterial infections that affect over one billion people and kill 500,000 people annually, most of whom live on less than two dollars per day. NTDs stigmatize, disable and inhibit individuals from being

able to care for themselves or their families, and many are fatal without treatment. As such, they are diseases of poverty that transcend sectoral and geographical boundaries and promote economic and social inequities.

USAID is deeply involved in control of seven “tool-ready” neglected diseases – those diseases for which appropriate diagnostics, treatments and/or vaccines exist. However, the few treatments that are available for these deadly diseases often date back to the colonial period and are inadequate by today’s standards. Based on its success in supporting the development of new tools for HIV/AIDS, malaria, and tuberculosis, USAID could play a key role in developing and adapting appropriate health products and interventions—including supporting field testing and introduction—and strengthening local health systems to more effectively combat deadly NTDs.

Technology Devices

More than any other federal agency, USAID is familiar with the conditions and circumstances that make public health work in the developing world unique. Delivering health interventions to those who need them in the developing world requires creative strategies and tools, which in many cases the private sector alone is unlikely to develop. USAID has stepped in and filled this gap, providing the research and development support necessary to ensure that medical devices appropriate to a developing-world context are created and made available.

One example of this work is USAID’s efforts to address the need for injection devices that can be used by untrained health care workers, and which do not increase the risk of infectious disease transmission. Working with private non-profit and for-profit partners, USAID supported the development of the prefilled single-use Uniject® injection device;² to date, more than 70 million Uniject devices have already been distributed.

Another challenge in the developing world is the maintenance of refrigeration throughout the supply chain for medicines and vaccines that must be kept below a maximum temperature to remain effective, and which should not be administered if this “cold-chain” has not been kept intact. To help address this challenge, USAID supported research and development leading to the creation and distribution of almost three billion “vaccine vial monitor” stickers that indicate visually when a vial of vaccine has been damaged by heat during shipment or storage. These devices help ensure that spoiled vaccines are not given to patients and also that good vaccines are not disposed of because of suspicion that they may have gone bad.

Contraceptive Technologies

Access to contraception contributes to improved child and maternal health, which in turn advances development. For this reason, USAID invests in the development of a range of contraceptive technologies designed to better enable families in the developing world to avoid unintended pregnancy, optimize birth spacing, and determine family size. USAID supports

² Uniject is a registered trademark of Becton, Dickinson & Co.

research aimed at developing new contraception technologies, as well as research designed to expand access to contraception in the developing world. For example, USAID has supported research on woman-initiated contraceptive vaginal rings and female condoms, technology designed specifically to deliver an injectable contraceptive in the developing-world context, and a system for educating couples about their fertility cycles. It should be noted that a majority of USAID's research and development work in this area focuses on contraceptive technologies that serve to prevent both pregnancy and sexually transmitted infections.

Maternal and Child Health Technologies

Mothers and children in the developing world continue to suffer from certain specific health burdens at rates far exceeding those in the developed world, and USAID recognizes that sustainable development advances cannot be achieved until this health burden is relieved. USAID understands that, while we already possess some effective tools for use in improving the health of mothers and children, more will be needed if we are to secure and expand our global efforts to improve maternal and child health.

To this end, USAID is deeply involved in the research and development of new tools designed to reduce the disease burden on women and children in the developing world. This includes USAID-supported research on methods for reducing neonatal death from infection by administering the drug gentamicin with the single-use, prefilled, auto-disable Uniject injection device. USAID is also exploring the use of the Uniject device to prevent maternal deaths from postpartum hemorrhage by administering the drug oxytocin, which reduces bleeding following childbirth. Additionally, respiratory and enteric infections continue to be the most prominent killers of children worldwide. USAID is working to develop new tools to reduce the toll of these diseases on the world's children through ongoing efforts to catalyze, coordinate, and provide financial support for early proof-of-concept clinical trials in impoverished populations in developing countries for vaccines to prevent diarrheal and respiratory diseases.

Laboratory Capacity

Over the course of decades of involvement in global health research, USAID has learned that with even a limited amount of recurring funds, it can maintain high-quality laboratories that support both national and international programs. Even relatively small amounts of USAID funds for ongoing laboratory work, including funds supporting quality control, can result in a significant improvement to local disease research and disease control efforts.

One example of USAID's efforts in this area includes the agency's hugely successful La Paz and Cochabamba, Bolivia-based programs focused on diarrheal disease diagnosis, STD diagnosis, and Chagas disease diagnosis and research. USAID's Chagas disease program was particularly important because of the country-specific morbidity and mortality associated with Chagas in the Cochabamba valley, in Tarija, Sucre, and other locales. USAID was the only donor active in this area, and supported critical vector control research on residual spray impact.

Conclusion

Without strong USAID support for research and development to inform and support the development and introduction of products specifically designed for the developing world, many critical health interventions would not reach or be used by those who need them most. Moreover, the benefits of global health research and development extend beyond their most immediate beneficiaries. In an increasingly connected world, reductions in infectious diseases abroad may reduce health risks to US citizens. High rates of infectious disease in developing countries can also pose risks to US economic and security interests. Developing-country populations trapped in disease and poverty can be vulnerable to instability, hindered from pursuing trade with developed countries, and unable to meet development goals or debt obligations. To protect US interests and strengthen our relations with allies and trading partners, it is essential that USAID support for research and development continues to ensure increased innovation and uptake of critical health interventions for the developing world.