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REPORT TO CONGRESS

Health-Related Research and Development Activities at USAID

An Update on the Five-Year Strategy, 2006–2010

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Acknowledgments

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Cover photo of Africare Senegal project courtesy of Namita Agravat.

PREFACE

I am pleased to present the U.S. Agency for International Development's (USAID's) 2010 *Report to Congress: Health-Related Research and Development Activities at USAID*. This report describes the Agency's ongoing commitment to science, technology, and research – getting the latest discoveries out of the lab and into communities to directly benefit the world's poor.

As we enter our 50th year, USAID is proud of its leading role in implementing President Obama's new vision for global development policy. The President's approach recognizes that sustainable development is a long-term proposition that will require game changing innovations and sustainable systems for meeting basic human needs.

The President's Global Health Initiative is a concrete manifestation of this new approach and will be reflected in future year reports to Congress. The Global Health Initiative will expand investments in transformative innovations by promoting medical research and development.

This year, we saw how much promise these research investments hold. In July, evidence from field trials showed that an antiretroviral microbicide gel could effectively reduce the risk of HIV infection of women by 39 percent. These trial results, which were celebrated on newspaper front pages around the world, represent a major milestone in the battle to contain the still expanding AIDS epidemic. The U.S. Government, through USAID, provided the financial support that made this trial possible. It serves as a powerful example of the impact U.S.-supported research can have in turning the tide against some the world's most intractable health challenges.

I welcome this opportunity to inform you of our latest research efforts in health and how they are contributing to real, lasting development gains. I thank Congress for its continued support of USAID and its health-related research agenda.

Dr. Rajiv Shah
Administrator, U.S. Agency for International Development

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Acronyms and Abbreviations

ACT	artemisinin-based combination therapy
AI	avian influenza
AMTSL	Active Management of the Third Stage of Labor
ART	antiretroviral therapy
ARV	antiretroviral drug
BCC	behavior change communications
CAPRISA	Center for the AIDS Program of Research in South Africa
CCM	community case management
CDC	U.S. Centers for Disease Control and Prevention
CHW	community health worker
CHX	chlorhexidine
CMAM	Community-based Management of Acute Malnutrition
CSHGP	Child Survival and Health Grants Program
DOTS	Directly Observed Treatment, Short-course
ENC	essential newborn care
EONC	essential obstetric and newborn care
EPT	Emerging Pandemic Threats
FP	family planning
FY	fiscal year
GDA	Global Development Alliance
GLC	Green Light Committee
GSK	GlaxoSmithKline Biologicals
HBB	Helping Babies Breathe
HTSP	Healthy Timing and Spacing of Pregnancies
IAVI	International AIDS Vaccine Initiative
iCCM	integrated community case management
IUD	intrauterine device
KMC	kangaroo mother care
LAC	Latin America and the Caribbean
LAM	Lactational Amenorrhea Method

LAPM	long-acting and permanent contraception method
M&E	monitoring and evaluation
MCH	maternal and child health
MDR-TB	multidrug-resistant tuberculosis
MMV	Medicines for Malaria Venture
MNCH	maternal, newborn, and child health
MNH	maternal and newborn health
MOH	Ministry of Health
MVDP	USAID Malaria Vaccine Development Program
NGO	nongovernmental organization
NHA	national health accounts
NIAID	National Institute of Allergy and Infectious Diseases
OR	operations research
ORS	oral rehydration solution
ORT	oral rehydration therapy
OVC	orphans and vulnerable children
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PM2A	Prevention of Malnutrition in Under 2s Approach
PMI	President's Malaria Initiative
PMTCT	prevention of mother-to-child transmission of HIV
PPH	postpartum hemorrhage
PrEP	pre-exposure prophylaxis
PVOs	private and voluntary organizations
QAPC	Quality Assurance Partnership Committee
QI	quality improvement
R&D	research and development
R2P	Research to Prevention
RDT	rapid diagnostic test
RH	reproductive health
RHIS	routine health information systems
RUTF	ready-to-use therapeutic food
SAM	severe acute malnutrition
SDM	Standard Days Method
STI	sexually transmitted infection

TB	tuberculosis
UNAIDS	Joint United Nations Program on HIV/AIDS
UNICEF	United Nations Children's Fund
USAID	U.S. Agency for International Development
WASH	water, sanitation, and hygiene
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research

Executive Summary

In 2006, the U.S. Agency for International Development (USAID) outlined for Congress its five-year health research strategy.[1] On an annual basis, the Agency's Research Report to Congress has reported on progress in the development and introduction of affordable health products, policies, and practices appropriate for addressing health-related concerns in the developing countries and countries in transition listed in Table 1 below. This 2010 *Report to Congress: Health-Related Research and Development Activities at USAID* is the final annual update on the results of the Agency's 2006–2010 health research strategy; in 2011, the report will provide an assessment of the five-year strategy as the foundation for a new strategy.

USAID assesses health conditions in developing countries and develops, tests, adapts, and introduces appropriate products and interventions within the context of strengthening local health systems. This role under the current health research strategy fits well within the objectives of two initiatives: the Global Health Initiative and Feed the Future.

To achieve the greatest health impact, USAID engages with multiple partners – including the U.S. Centers for Disease Control and Prevention (CDC), the National Institutes of Health, the Department of Defense, multilateral and donor agencies, foundations, partner country governments, universities, nongovernmental organizations, and commercial-sector partners – to address country-specific issues, resolve global challenges, and establish the evidence base for the development of consensus on technical and policy issues.

For the first time, the 2010 Research Report to Congress includes a description of research on Emerging Public Health Threats, reflecting a need for the development of comprehensive aggressive disease detection and response capacities, particularly in geographic areas where new, emerging, or re-emerging disease threats that have an impact on human health are likely to surface.

Maternal and Newborn Health

Each year, about 358,000 women die due to preventable pregnancy- and childbirth-related complications; postpartum hemorrhage is the leading direct cause of maternal mortality in developing countries. Other major causes include pre-eclampsia and eclampsia, sepsis and unsafe abortions, and obstructed labor. USAID's success in scaling up the Active Management of the Third Stage of Labor in 40 countries has led to further studies on

1 U.S. Agency for International Development. *Report to Congress: Health-Related Research and Development Activities at USAID*. 2006. Available from http://pdf.usaid.gov/pdf_docs/PDACH111.pdf.

Table 1. Countries with USAID Health-Related Research and Development Activities

Afghanistan	Cameroon	Guinea	Namibia	South Africa
Angola	China	Guyana	Nepal	Swaziland
Argentina	Côte d'Ivoire	Haiti	Nicaragua	Tanzania
Armenia	Democratic Republic of the Congo	Honduras	Niger	Thailand
Bangladesh		India	Nigeria	Uganda
Benin	Ecuador	Indonesia	Pakistan	United States
Botswana	Egypt	Kenya	Paraguay	Vietnam
Brazil	Ethiopia	Madagascar	Peru	West Bank and Gaza
Burkina Faso	Fiji	Malawi	Philippines	Yemen
Burundi	Ghana	Mali	Rwanda	Zambia
Cambodia	Guatemala	Mauritania	Senegal	Zimbabwe

Key results of the 2006–2010 research strategy to date include the following:

- In 2010, The Center for the AIDS Program of Research in South Africa (CAPRISA) 004 trial provided the first-ever proof of concept that a microbicide – Tenofovir 1-percent vaginal gel – could safely and effectively reduce the risk of heterosexual transmission of HIV from men to women. Five other promising microbicide candidates have advanced into the final stages of clinical testing for their safety, effectiveness, and acceptability.
- A USAID-supported International AIDS Vaccine Initiative (IAVI) study provided the first evidence that a new vaccine technique using a replicating rhesus cytomegalovirus vector could effectively control viral replication in vaccinated animals. These findings have prompted IAVI to establish a clinical development program for human cytomegalovirus-vector vaccine candidates.
- Recent successes in formulating new drugs for malaria include the development of a dispersible pediatric lumefantrine-artemether formula and the submission of two new novel antimalarial drugs for regulatory approval.
- In the last year, separate studies have provided proofs of concept of vaccines against both the blood and liver stages of malaria parasites.
- USAID supported the research and translation into global policy of a new recommendation for use of a light-emitting diode fluorescence microscopy as well as a procedural shift from three to two smears to diagnose tuberculosis, an approach that promises to increase case detection, decrease wait time, and reduce costs for patients and laboratories.
- USAID supported a promising clinical trial to test the effectiveness, safety, and acceptability of the Nestorone®/Ethinyl Estradiol contraceptive vaginal ring, a female-controlled hormonal method that lasts for up to 12 months. Results support USAID's continued efforts to develop a user-controlled, long-acting contraceptive that does not require daily attention from women or the availability of trained health providers for insertion or removal.
- USAID-supported studies showed that the Standard Days Method (SDM), a simple, highly effective fertility awareness-based method, could be provided safely and effectively at all levels of the health system. SDM has been introduced in the health systems of more than 25 countries.
- USAID introduced and expanded the Active Management of the Third Stage of Labor, a lifesaving practice conducted after labor and birth to prevent postpartum hemorrhage (PPH) in women, in 40 high-mortality countries and continues to apply new research results to reduce PPH at the community level, including the use of misoprostol by community health workers.
- In South Asia, USAID-supported studies demonstrated the effectiveness, cost-effectiveness, and feasibility of community-based care in promoting neonatal health and survival. This key evidence informed a new World Health Organization (WHO)/UNIICEF policy guidance on newborn care at the community level.
- USAID linked program implementation with operations research to identify evidence-based solutions for increasing the availability and uptake of zinc/oral rehydration solution (ORS) treatment to reduce diarrhea-related morbidity and mortality. More than one dozen countries have introduced and scaled up zinc treatment in association with oral rehydration therapy/ORS.
- In Pakistan, USAID-financed studies on the effectiveness of community-based treatment of severe pneumonia provided the evidence base for new WHO guidelines for outpatient management of severe pneumonia and are likely to lead new guidance on community management of severe pneumonia.
- USAID established and strengthened postmarketing surveillance systems to sample and test the quality of medicines in Latin America, Africa, and Southeast Asia, raising awareness on the substandard and counterfeit malaria drug problem in developing countries.

strengthened approaches to prevent PPH, including research in Nepal that resulted in the Ministry of Health and Population's nationwide expansion of community-based PPH prevention using misoprostol. Research, policy, and program efforts also have focused on the second biggest direct cause of maternal mortality: pre-eclampsia/eclampsia. In 2009, nearly 8.1 million children under the age of 5 died worldwide. An estimated 41 percent of these deaths were among newborn infants in their first month of life. Research on newborn health has brought promising results in the use of training and resuscitation devices for community health workers (CHWs) to prevent birth asphyxia, reduce neonatal infections using topical cleansing of the umbilical cord with a 4-percent chlorhexidine solution, and administer antibiotics at the first sign of a suspected neonatal infection.

Child, Environmental, and Urban Health

Pneumonia, diarrhea, and malaria are among the leading causes of preventable death in children under 5. Many of these deaths can be avoided through case management; clean water and sanitation and hygiene improvement interventions; and malaria prevention and treatment. USAID has focused on key access barriers to community-level care. In the past year, USAID-supported research in Zambia demonstrated the effectiveness and feasibility of CHWs in managing pneumonia and malaria with the aid of rapid diagnostic tests, showing that these methods correctly diagnosed and treated children with malaria. The use of these tests can reduce overuse of antimalarial drugs and subsequent drug resistance, cut down on drug and program costs, and provide children with early and appropriate treatment for pneumonia and malaria. Studies of Integrated Community Case Management of child illness in Rwanda and Senegal showed demand for and significant use of community-level treatment services. A USAID-supported program in Benin demonstrated the effectiveness of building upon an existing oral rehydration solution (ORS) brand to launch a new branded kit that combined both ORS and zinc to treat diarrhea. At the end of the program, 31 percent of caregivers had used zinc to treat their child during an episode of diarrhea.

Nutrition

Nearly half of all maternal and child deaths are attributable to undernutrition. USAID supports the development of evidence-based and innovative new approaches that will increase access and improve outcomes for the most vulnerable populations. This includes a focus on vitamin A deficiency prevention and control, anemia prevention and treatment, Community-based Management of Acute Malnutrition, and dietary quality and diversity. USAID-supported clinical effectiveness studies in Malawi are assessing improved formulations of ready-to-use therapeutic food for the treatment of moderate acute malnutrition. Concurrently, USAID is supporting effectiveness trials in Bangladesh and Guatemala on the impact of lipid-based nutrient supplements for the prevention of chronic undernutrition in children.

Family Planning and Reproductive Health

Enabling couples through family planning (FP) services to determine whether, when, and how often to have children is vital to safe motherhood and healthy families. FP reduces unintended pregnancy, which consequently reduces abortion, maternal and child mortality, and mother-to-child transmission of HIV/AIDS. USAID's FP and reproductive health research develops, tests, introduces, and scales up new and improved technologies, tools, and approaches to decrease unintended pregnancies and prevent the transmission of HIV and other sexually transmitted infections. USAID has achieved important progress in its strategy to develop and evaluate new contraceptive methods, including the 12-month combined Nestorone®/Ethinyl Estradiol contraceptive vaginal ring – the first-ever long-acting hormonal contraceptive that allows women complete control to determine when to start and discontinue use. Preliminary results indicated that this method is effective in preventing pregnancy, safe, highly acceptable to users, and reversible. Significant progress also was achieved with the novel, one-size-fits-most female barrier method – the SILCS diaphragm, a silicone barrier contraceptive device. USAID studies in Uganda, Madagascar, and Malawi confirm that community-level workers are able to provide the popular injectable contraceptive Depo-Provera as safely and effectively as doctors or nurses, thus presenting new opportunities for improving access to this method. Additionally, the feasibility and acceptability of providing FP information and education via cell phone text messaging was established.

HIV/AIDS

An estimated 33 million people worldwide are living with HIV, more than half of them women. USAID supports biomedical, applied, operations research, and public health evaluations to improve HIV/AIDS intervention programs aimed toward lessening the burden of HIV/AIDS in developing countries. The three areas of HIV/AIDS research support are microbicides research, HIV vaccine research, and public health evaluations. The CAPRISA 004 microbicide trial provided landmark results proving that a vaginal gel used regularly can prevent both HIV

transmission and herpes simplex virus infection. Confirmatory trials are being planned in order to advance the use of microbicides as a female-controlled method of effective HIV prevention. The USAID-supported International AIDS Vaccine Initiative provided two breakthrough findings: (1) powerful antibodies that block the majority of HIV strains and (2) the first evidence that a new vaccine technique using a replicating vector could control HIV effectively; these findings are guiding development of new vaccine candidates.

Malaria

Malaria remains one of the major public health problems in Africa. It is estimated there are between 300 million and 500 million cases and about 900,000 deaths from the disease each year, with 90 percent of those deaths in African children under 5 years of age. Though we have seen a decrease in the incidence and prevalence of malaria in areas where proven prevention and treatment strategies have been applied and a significant reduction in under-5 child mortality rates, increased resistance to both antimalarial drugs and insecticides has created a need for new technologies and tools that can improve and maintain malaria control efforts. USAID-supported vaccine and drug research and development have provided new evidence of the feasibility of improved vaccines for prevention and of improved antimalarial drugs and drug formulations for treatment. Recent successes in new drug formulation include the development of a dispersible pediatric formula of lumefantrine-artemether and the submission of two new novel antimalarial drugs for regulatory approval. In the last year, separate studies have provided proofs of concept of vaccines against both the blood and liver stages of malaria parasites. We are also searching for answers to key operational questions such as the feasibility of using rapid diagnostic tests for malaria at the community level.

Tuberculosis

Tuberculosis (TB) continues to be a major global health problem, with around 9 million new cases and approximately 1.8 million TB-related deaths reported each year. The TB epidemic is worsened by the HIV epidemic and the emergence of multidrug-resistant TB (MDR-TB), of which 400,000 to 500,000 new cases develop each year. USAID is supporting research to improve the performance and public health impact of country-level TB programs while mitigating the risks of drug resistance by reducing diagnostic delay as well as the duration and increasing efficacy of treatment. USAID funded a series of studies to determine how to maximize the efficiency and effectiveness of new diagnostic tools in TB program settings and to evaluate their impact on TB control. USAID is supporting the implementation of a clinical trial using a shorter treatment regimen – nine months instead of 18 or more – for the treatment of MDR-TB; this regimen demonstrated cure rates exceeding 80 percent in a pilot program. If the USAID-supported clinical trial reproduces this result in various countries, it will revolutionize the management of MDR-TB and have a major impact on the TB epidemic. USAID also is contributing to the development of new TB drugs by supporting late-stage trials of four new drugs that could shorten the course of TB treatment, thus increasing treatment adherence and reducing the chances for developing MDR-TB.

Emerging Pandemic Threats

USAID's Emerging Pandemic Threats program seeks to pre-empt or combat, at their source, emerging zoonotic disease threats that could have a significant impact on human health. Research in this area supports a comprehensive surveillance capacity for emerging disease threats by complementing traditional "syndromic surveillance" methods with the development of a new "predictive surveillance" model for early detection of viruses and other pathogens before they can spread to humans. This model will consider environmental factors, potential points of disease transmission, and advances in genomics and informatics to classify new harmful organisms.

Health Systems Strengthening

USAID's approach is to look for constraints in quality, accessibility, or affordability and develop interventions to address key gaps and barriers. Illustrative of this approach is the Agency's work on quality improvement: An early leader in applying quality improvement approaches, USAID is supporting more than 30 new quality improvement collaboratives, an approach that involves health care teams improving performance without additional material resources. In the last year, USAID supported a retrospective analysis of 27 quality improvement collaboratives in 12 countries; after introducing identified changes, the teams achieved performance levels of 80 percent or higher in 87 percent of the 135 measures of compliance. Performance levels were sustained above 80 percent for an average of 13 months. These results indicate that teams participating in a collaborative approach can rapidly achieve significant sustainable improvements in quality of care.

Maternal and Newborn Health

Issues and Rationale

Each year, about 358,000 women will die from preventable complications during pregnancy and childbirth. An estimated 87 percent of maternal deaths take place in sub-Saharan Africa and South Asia. Postpartum hemorrhage (PPH) continues to be the leading direct cause of maternal mortality in developing countries, followed by pre-eclampsia and eclampsia, sepsis, unsafe abortions, and obstructed labor. High-risk pregnancies due to poor birth spacing as well as the young age of the mother contribute to both maternal and child mortality.

Despite the steady decline in child mortality rates worldwide, an estimated 8.1 million children under 5 died in 2009. About 41 percent of these deaths were among newborn infants in their first month of life. Newborn deaths are caused mainly by severe infection (sepsis or pneumonia, diarrhea, and tetanus), preterm births, asphyxia, obstructed labor, and congenital abnormalities. Low birthweight is the most important indirect cause of neonatal mortality.

Areas of Research and Introduction

Healthy Timing and Spacing of Pregnancies to Ensure Healthy Birth Outcomes

USAID continues to support research and analyses to better understand how to prevent high-risk pregnancies, implement effective service delivery strategies, and adapt counseling and family education approaches to different country settings to reach women and girls in need.

A USAID study of the contribution of increased contraceptive use to maternal mortality reduction in 45 developing countries found that increased used reduces the total number of births, and thus women's potential exposure to childbirth-related health threats. In addition, it reduces the number of high-risk births. Consequently, when contraceptive use in a country rises to 80 percent, the percentage of births with any risk drops to nearly 35 percent.[1] USAID is using these findings to develop evidence-based counseling tools to reach women and girls in all high-risk groups.

In Nepal, USAID research documented that counseling on Healthy Timing and Spacing of Pregnancies (HTSP) interventions positively influenced two-year family planning (FP) continuation rates. The results of this work will be used to plan the scale-up of programs in Nepal. In rural Bangladesh, a study is testing the feasibility of integrating postpartum FP/HTSP counseling into a community-based maternal and neonatal program. Preliminary analysis found that a focus on FP's role in health outcomes facilitated client-provider discussions. It also found that community health workers (CHWs) are able to deliver FP and HTSP messages. This study is expected to be completed in 2012.

Another study in Bangladesh is examining eight different pregnancy timing and spacing patterns and their association with health outcomes. USAID will continue to build on these study findings to strengthen family planning,

Spotlight: Moving Research to Practice

USAID has launched programs to train Muslim religious leaders on HTSP in Kenya, Nigeria, Bangladesh, Yemen, and Pakistan. In 2010, USAID, in collaboration with the Pakistan Ministry of Population Welfare, brought together religious leaders from six different Islamic sects – Shia, Ahle, Hadith, Deobandi, Barelvi, and Sunni – for the first time. The purpose of this workshop was to educate the religious leaders about the role of modern contraceptives in ensuring that pregnancies are timed and spaced to occur at the healthiest times of a woman's life, thus helping to achieve the best health outcomes for women, newborns, and children. Approximately 100 additional religious leaders will be trained in each of Pakistan's 134 districts by the end of 2010. One religious leader from Multan said, "Intrafaith harmony and joint understanding to address the high-population problem are two main achievements of this workshop. The workshop provided us all a unique opportunity to arrive at a uniform line of action and thought regarding birth spacing." Another religious leader said that the workshop was "instrumental in removing doubts and misperceptions regarding family planning…[and] we now realize that spacing between pregnancies is the fully Islamic way of living."

1 Stover, J. & Ross, J. (2010). How increased contraceptive use has reduced maternal mortality. *Maternal Child Health Journal*, *14*(5), 687–695. Published online July 31, 2009.

Maternal and Newborn Health Research Strategy 2006–2010

Total FY10: $9,109,080	
Strategy Themes	**Areas of Research and Introduction: Five-Year Strategy**
Healthy Pregnancy and Birth Outcomes	Determine the health impact of Healthy Timing and Spacing of Pregnancies Develop and support the implementation of effective communication, education, and service delivery activities for Healthy Timing and Spacing of Pregnancies
Assessment of Birth Care and Outcomes	Determine impact of cesarean section on birth outcome Conduct global systematic review of direct causes of maternal mortality Review physical, psychological, and economic consequences Determine impact of family planning in different settings on maternal mortality Evaluate effectiveness and cost-effectiveness of approaches
Maternal Mortality and Morbidity Measurement Tools	Develop standardized criteria and effective tools for defining and measuring maternal mortality and morbidity
Effective Pregnancy and Birth Interventions and Introduction	Conduct stability studies, scale up production, and launch in multiple countries uniject oxytocin Determine the non-inferiority of simplified Active Management of the Third Stage of Labor for postpartum hemorrhage prevention Review determinants of postoperative fistula repair practices Develop and introduce evidence-based approaches to pre-eclampsia and eclampsia
Neonatal Research and Newborn Care Practices	Complete effectiveness and cost-effectiveness studies and implement and evaluate minimal package for essential newborn care Determine effectiveness and cost-effectiveness studies, alternative formulations, and delivery strategies for treatment and prevention of infections Evaluate and implement community-based kangaroo mother care to determine strategies for care of low-birthweight infants Field test and scale up new global curriculum and work with UNICEF and commercial companies to distribute low-cost devices for resuscitation clinical capacity and device availability
Integrated Maternal and Newborn Health Programs	Develop scalable, cost-effective approaches for integrating maternal and neonatal health services

maternal and child health (MCH) programs, and women- and girls-centered care.

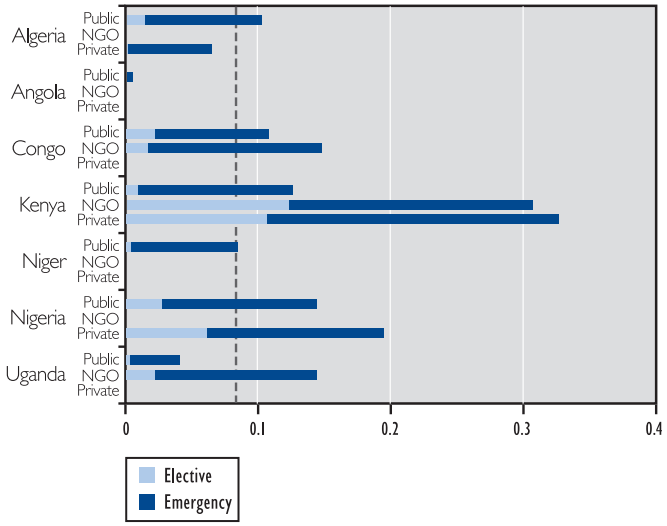
To address young adolescent pregnancy and child marriage, in Bihar, India, USAID is evaluating the impact of a multisectoral, gender-equity approach on increasing marriage age, delaying the first pregnancy, and improving the timing and spacing of subsequent pregnancies.

Evidence-based HTSP guidelines have been institutionalized into national policies, protocols, and curricula in Angola, Guinea, and Kenya, as well as in Nepal through the country's pending National Safe Motherhood Act.

Assessment of Birth Care and Outcomes

The ideal proportion of cesarean sections ranges between 5 percent and 15 percent of births. Low cesarean section

Figure 1. Proportion of Elective and Emergency Cesarean Deliveries by Facility Type and Country



Source: Shah, A., et al. (2009). Cesarean delivery outcomes from the WHO global survey on maternal and perinatal health in Africa. *International Journal of Gynecology & Obstetrics*, 107(3), 191–197.

Note: Broken line denotes median cesarean delivery rate for all facilities.

rates are indicative of health systems with insufficient access to emergency obstetric care; conversely, rates much higher than the optimal range are suggestive of weak elective indicators for surgery that may contribute to adverse outcomes and are a financial drain on the resources of weak health systems. A USAID-supported World Health Organization (WHO) global survey documented an exponential growth in cesarean deliveries within private, public, and nongovernmental settings in Latin America and Asia. The study found cesarean delivery rates of 33 percent in Latin America and 27.3 percent in Asia and documented an association between high rates of surgery and adverse outcomes for both women and newborns. In Africa, cesarean rates in facilities were very low, and emergency cesareans often were performed too late to prevent death (Figure 1). These findings will be used to guide policies and programs that address the use of cesarean sections in developing countries.

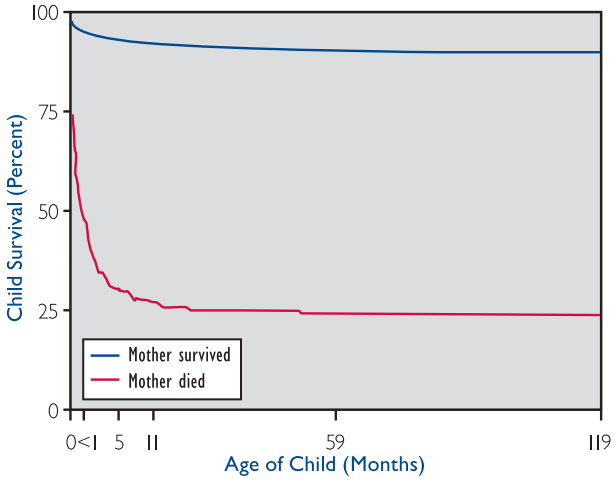
Building on this work, USAID has initiated a 16-country analysis of Demographic and Health Survey data on the growth of private facility delivery care. This analysis will provide insights into private birth facility utilization and coverage and costs to underserved populations.

In Bangladesh, a longitudinal study of the impact of maternal morbidity documented the effects of maternal death on child survival and social well-being. It found that a woman's death prior to a child's 10th birthday reduced the probability of the child's surviving to the age of 10 from 89 percent to 24 percent (Figure 2). Children aged 2–5 months who lost their mothers were 25 times more likely to die than those whose mothers were alive. In addition, compared with their counterparts, children who lost their mothers were likely to have less education. These findings highlight the double burden associated with maternal death and the role that reducing maternal mortality plays in improving child survival.

Macropolicy interventions such as cash transfers, pay for performance, and the provision of health insurance may directly or indirectly have an impact on women's access to and utilization of health services. A USAID-supported study will examine the intended and unintended consequences of these mechanisms on health-seeking behaviors and the health system's capacity to deliver care.

The ability to recognize the signs and symptoms of an illness, its perceived severity, and maternal health care-seeking behaviors during pregnancy and the postnatal period are associated with maternal-newborn mortality and morbidity outcomes. A USAID-supported study will assess the effectiveness of existing communication strategies – CHWs, facility outreach, and community mobilization – in influencing the ability of families to recognize maternal-newborn complications and seek appropriate care.

Figure 2. Kaplan-Meier Survival Curve from Birth by Survival Status of the Mother



Source: Ronsmans, C., et al. (2010). Effect of parent's death on child survival in rural Bangladesh: A cohort study. *The Lancet*, 375(9730), 2024–2031.

A final component of USAID's effort to improve utilization of skilled care at birth entails a study to identify contributors to the mistreatment of women around the time of labor and delivery in facilities.

Maternal Mortality and Morbidity Measurement Tools

Lack of standardized criteria and effective tools for defining and measuring maternal mortality and morbidity have led to inconsistencies in the way maternal deaths are classified and reported worldwide. USAID supports the development and refinement of tools to improve the measurement of maternal mortality and morbidity. Better data and direct measurement of maternal mortality will decrease the application of the proxy measures that currently are used to assess maternal health interventions, quality improvement efforts, economic impact, and societal outcomes related to maternal death.

In partnership with WHO, USAID funded the revision of the maternal death classification system to standardize the cause distribution of maternal deaths within and across countries. This analysis established a standard definition and classification criteria for a maternal "near miss": a woman who nearly dies but survives a complication that occurs during pregnancy or childbirth, or within 42 days of termination of pregnancy. The maternal "near miss" is a useful indicator for identifying severe acute maternal morbidity and addressing weaknesses as well as strengths in obstetric care. USAID supported the development of a guidance tool for the application of the maternal death classification system to research studies and national vital statistics systems.

Effective Pregnancy and Birth Interventions

Postpartum Hemorrhage Prevention

Postpartum hemorrhage is a leading cause of maternal mortality in low-income countries, accounting for more than 25 percent of maternal deaths. USAID is spearheading a global effort to prevent PPH through an approach known as Active Management of the Third Stage of Labor (AMTSL), in which oxytocin, controlled cord traction, and uterine massage after delivery of the placenta are used to reduce blood loss and transfusions.

Since 2004, USAID has been working with professional societies, researchers, United Nations agencies, nongovernmental organizations (NGOs), and the private sector to introduce and expand the safe and effective use of AMTSL in at least 40 high-mortality countries. Nationally representative surveys of facility-based deliveries in 10 countries found limited use of AMTSL – use of this intervention was observed in only 0.5 to 32 percent of deliveries – and revealed multiple deficiencies in practice. These findings have been used to encourage Ministries of Health (MOHs), international partners, and policymakers to ensure that safe motherhood guidelines and practices include AMTSL.

USAID also is advancing research to simplify AMTSL, undertaking new product development, and determining the safest and most feasible strategies for introduction of these new products. A USAID-funded WHO trial of an estimated 20,000 patients is testing a simplified version of AMTSL in eight hospitals in Argentina, Egypt, India, Kenya, South Africa, the Philippines, Thailand, and Uganda. If this simplified version of AMTSL, which excludes controlled cord traction, is comparable to the full AMTSL package, the complexities of training workers in health facilities and communities would be reduced significantly, and coverage of AMTSL could be expanded more rapidly.

Misoprostol is an effective uterotonic to prevent postpartum bleeding; unlike oxytocin, it can be administered orally and does not require refrigeration. USAID-supported studies in Nepal, Afghanistan, and Senegal have shown the feasibility of community-based distribution of misoprostol, indicating that the drug should be considered when oxytocin is not available at the community level. In Nepal, where 82 percent of women do not give birth in health facilities, a USAID-supported study showed that it is feasible to achieve high-population coverage of misoprostol through trained community health volunteers under the Government primary health care system. In one district, coverage of drugs to prevent postpartum bleeding rose from less than 12 percent to more than 74 percent. The biggest gains were among women who were poor, illiterate, and living in remote areas. The study also showed that a community-based strategy to expand the use of misoprostol can help to increase institutional delivery rates. Based on these study results, the MOH is expanding community-based PPH prevention using misoprostol for the entire country. USAID is partnering with the Government of Nepal to monitor this national expansion.

Uniject™ is a simple, single-dose, non-reusable injection device that can be used by trained health workers in home deliveries and remote health settings. Administering oxytocin in the Uniject™ device to prevent postpartum bleeding has the potential to increase the use of AMTSL, as it reduces the logistical limitations that often are associated with the regular injection process. Since receiving regulatory approval in 2008, the oxytocin in Uniject™ device has been available for use in field evaluations and pilot introduction efforts in community settings. USAID

is supporting studies to evaluate the use of the oxytocin in Uniject™ device in Nicaragua, Guatemala, and Honduras. With USAID's support, a second pharmaceutical manufacturer received regulatory approval for the oxytocin in Uniject™ device in 2009.

Pre-eclampsia/Eclampsia

USAID is undertaking a concerted research and introduction effort to reduce maternal pre-eclampsia/ eclampsia. Pre-eclampsia/eclampsia causes high blood pressure in women, which adversely affects blood flow to the placenta and can lead to life-threatening complications, including poor fetal growth and premature birth, as well as seizures and coma in the mother. When hemorrhage as a cause of maternal death declines, as it has in Latin America and the Caribbean (LAC), pre-eclampsia/ eclampsia becomes the leading cause of maternal death; it accounts for 26 percent of maternal deaths in the LAC region as well as 9 percent in Asia and Africa. USAID is working to develop, introduce, and scale up evidence-based, comprehensive intervention packages to prevent and manage pre-eclampsia/eclampsia in low-resource settings and identify technical and operational factors that will facilitate program implementation.

USAID is supporting a multicenter, multicountry study designed to identify biomarkers for pre-eclampsia/ eclampsia. The study will assess the predictive ability of selected biomarkers – both angiogenic and non-angiogenic – for pre-eclampsia/eclampsia as well as the feasibility of their use in low-resource settings. Promising biomarkers will be used to develop affordable pre-eclampsia/eclampsia screening interventions specifically designed for developing countries.

USAID is contributing to the development of an outcome-predictor tool that identifies pregnant women who are at high risk for complications of pre-eclampsia/ eclampsia. The proposed tool being tested in eight countries is a simplified symptom- and sign-based instrument especially designed for poorly resourced settings. An interim analysis indicates that it is feasible to develop the model. Once the tool is validated, this tool may be converted into a handheld, pictographic device for use in rural and remote settings to predict the likelihood of adverse outcomes based on the woman's clinical status. This would enable more timely case identification and assessment of case severity, as well as appropriate care decisions.

A USAID-supported multicountry quality of care survey is assessing pre-eclampsia/eclampsia care in health facilities. The survey is documenting prevalence of use, quality of implementation, and barriers to the performance of pre-eclampsia/eclampsia screening and management interventions; the results will provide baseline data on pre-eclampsia/eclampsia case identification and treatment practices. The survey also will assess other key maternal and newborn health interventions: AMTSL to treat PPH, partograph use during prolonged/obstructed labor, infection prevention, essential newborn care (ENC), and resuscitation in cases of birth asphyxia. Findings from this study will be used to guide quality of care improvement activities and policies within facility, district, and national fronts. Countries participating in this survey include Ethiopia, Kenya, Tanzania, Rwanda, Zimbabwe, Madagascar, Paraguay, and Indonesia.

Fistula Repair

Obstetric fistula is a condition in which an abnormal opening (or fistula) in the birth canal forms as a result of prolonged, obstructed labor and lack of emergency obstetrical care. An untreated fistula case can cause severe lifelong complications and disability and is a leading cause of maternal morbidity.

USAID is supporting a prospective facility-based study in Bangladesh, Guinea, Niger, Nigeria, Rwanda, and Uganda to identify factors that contribute to positive postoperative outcomes of fistula repair surgery. The study results will be used to identify potential new areas in need of investigation and opportunities to strengthen and standardize high-quality care.

Complementary to this work, a randomized controlled trial will test the efficacy and safety of using short-term catheterization after fistula repair rather than longer-term catheterization. Short-term catheterization has the potential to reduce hospital stays for women, free up bed space at facilities, and reduce costs, potentially allowing more women to receive clinical care.

USAID is supporting a multicenter retrospective record review of indications for cesarean deliveries in health facilities supported by fistula care programs. Since the provision of a safe and timely cesarean section is a key fistula prevention strategy, assessing the number of cesarean deliveries that are performed due to an indication of obstructed labor will provide insight into the number of averted fistulas. Findings from this study will be used to address challenges to data reporting and help enhance monitoring and evaluation (M&E) systems for emergency obstetric services to prevent death, fistula, and other complications.

Spotlight: Moving Research to Practice

USAID has supported the development and validation of newborn resuscitation training materials and devices used to develop the American Academy of Pediatrics' Helping Babies Breathe (HBB) training curriculum. In June 2010, USAID launched a public-private partnership called the HBB Global Development Alliance (GDA), along with several partners – the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Laerdal Medical AS, the American Academy of Pediatrics, and Save the Children – in collaboration with other organizations, including UNICEF and WHO. The goal of this GDA is to reduce newborn mortality by expanding access to the HBB program, strengthening health systems, and promoting global commitment and resources for lifesaving newborn care. The GDA has begun introducing HBB in multiple countries and offers evidence-based training and technical support on newborn resuscitation and high-quality, affordable resuscitation devices to birth attendants in low-resource settings. USAID implements the HBB activities through its implementing partners: the Maternal and Child Health Integrated Program, Health Care Improvement, HealthTech, and CORE Group.

Neonatal Research and Newborn Care Practices

A recent article in *The Lancet*[2] noted USAID's seminal role working to focus global attention on the issue of newborn survival as well as its investments in establishing the research foundation for action in this area.

Essential Newborn Care

USAID-supported research studies have established the groundwork for community-based ENC. Current USAID-supported research in this area seeks to document and assess efforts to expand ENC in country-level MCH systems.

An assessment of ENC programs in Asia and Africa highlighted the role of both program coverage level and the ratio of CHWs per population in achieving significant impact. Programs varied significantly in the degree to which they were able to facilitate home care, increase family-initiated care-seeking behaviors and community mobilization, and train CHWs. The study concluded that implementers must understand fully the program context and dynamics in order to achieve substantial changes in practices.

Treatment and Prevention of Newborn Infections

Approximately one-third of the 3.1 million neonatal deaths that occur each year can be attributed to infections that develop into life-threatening conditions. USAID-supported research is strengthening the evidence base on infection management in young infants, especially in community-based settings.

USAID-supported research has shown that topical cleansing of the umbilical cord using a 4-percent chlorhexidine (CHX) solution – a low-cost, readily available antiseptic drug – reduces the risk of neonatal death from infections. A USAID-supported study in Bangladesh assessed the effectiveness and feasibility of a one-day versus seven-day application of CHX within a community setting and measured the impact of these regimens on newborn mortality and morbidity. Results of this study, expected in late 2010, will contribute to the evidence base on the use of CHX cord cleansing to prevent newborn infections in community-based settings. Preliminary results from meta-analysis of three CHX trials in Bangladesh, Nepal, and Pakistan indicate a positive effect of CHX in reducing all-cause neonatal mortality during the first week of life.

A parallel research effort assessed low-cost scalable approaches to delivering CHX to families with neonates in Bangladesh. Findings indicated a broad acceptance of and demand for CHX in the study communities. For CHX to be effective, families should obtain it prior to delivery and apply it correctly, as soon as possible after delivery.

Approximately one-third of newborn deaths can be attributed to infections caused by birth in unhygienic conditions. A multicountry trial supported by USAID, in partnership with the Bill & Melinda Gates Foundation; Save the Children/Saving Newborn Lives program; and WHO, is researching different combinations of oral and intramuscular antibiotic regimens for simplified treatment of newborn sepsis in the community. USAID is supporting study sites in Bangladesh and Pakistan to test the safety, effectiveness, and acceptability

2 Shiffman, J. (2010). Issue attention in global health: The case of newborn survival. *The Lancet*, 375(9730), 2045–2049.

of implementing treatment regimens in periphery facilities and the community.

Gentamicin in Uniject™, a commonly used antibiotic, can be administered by trained CHWs and trained birth attendants at the first sign of a neonatal infection, along with complementary antibiotics to ensure the timely delivery of treatment in peripheral health care settings and homes. Preliminary data from Nepal support the feasibility and acceptability of the use of the device for the management of neonatal sepsis. USAID is supporting efforts to facilitate marketing of the Gentamicin in Uniject™ device in order to expand the use of this promising intervention.

Strategies for Care of Low-Birthweight Infants

Kangaroo mother care (KMC), or skin-to-skin care, is an approach practiced in hospitals in developed and some developing countries to care for low-birthweight infants (less than 2,500 grams). USAID is working to build the evidence base and implementation strategy for KMC use at the health facility and community levels through its introduction into facility settings in Rwanda, Nigeria, Malawi, Nepal, the Democratic Republic of the Congo, India, and Bangladesh. At the community level, USAID is supporting a study to define community-based KMC, develop an appropriate implementation strategy, design tools for effective M&E, and also is conducting feasibility studies in Bangladesh and Malawi.

Increasing Availability of Resuscitation Devices

Each year, 10 million babies suffer from birth asphyxia; 10 percent of these newborns do not survive. Reducing birth asphyxia requires that appropriate technologies are available to birth attendants trained in neonatal resuscitation.

A USAID-supported study in Zambia demonstrated the effectiveness of resuscitation training as a component of neonatal care in the community. Traditional birth attendants were trained to prevent hypothermia, initiate treatment for sepsis, and manage birth asphyxia using simple practices and devices. Study data found 40 percent fewer neonatal deaths in newborns tended to by trained traditional birth attendants than in control groups. The study site now has been converted into a standing program within that district to train traditional birth attendants and other CHWs.

An evaluation of a Helping Babies Breathe program in Kenya on birth attendants' recognition of asphyxia and appropriate neonatal resuscitation responses found a statistically significant increase in knowledge, with 98

Key Partners in Maternal and Newborn Health Research and Introduction

Abt Associates
Bill & Melinda Gates Foundation
Boston University
Concern Worldwide
CORE Group
EngenderHealth
European Commission
Futures Group
Harvard School of Public Health
ICDDR,B (Bangladesh)
ICF Macro
International Aid
International Confederation of Midwives
International Federation of Gynecology and Obstetrics
International Rescue Committee
Jhpiego
Johns Hopkins University
John Snow, Inc.
National Institutes of Health
Partner government ministries of health
PATH
Pathfinder International
Save the Children/Saving Newborn Lives program
Schering-Plough
The Partnership for Child Health Care, Inc./BASICS
U.K. Department for International Development
UNFPA
UNICEF
University of Aberdeen (Scotland)
University Research, Co., LLC
Wellcome Trust
World Health Organization
World Relief
Wyeth

percent of participants passing the bag-and-mask ventilation skills test. Close to 300 birth attendants – including CHWs, traditional birth attendants, health facility nurses, reproductive health/FP nurses, and clinical officers – have been trained, with more than two dozen newborns resuscitated in a six-month period. As a result of this study, the Government of Kenya intends to scale up the newborn resuscitation Helping Babies Breathe program nationally. In addition, a similar effort is taking place in Bangladesh.

USAID is supporting a WHO systematic review of the evidence for basic newborn resuscitation in resource-limited settings. This review is anticipated to result in revised WHO policy and guideline materials designed for resource-limited settings.

Integrated Maternal and Newborn Health Programs

Despite the existence of evidence-based maternal and newborn interventions, limited access to skilled care, the absence of a defined postnatal care package, and the lack of an integrated community-to-facility maternal and newborn health (MNH) service delivery system undermine efforts to reduce mortality. While the risks are known, the postpartum and postnatal period receives less attention from health care providers than pregnancy and childbirth.

USAID is supporting research to develop an integrated, scalable, and affordable MNH intervention that can improve coverage and access to quality health care services. Study sites in sub-Saharan Africa will identify opportunities to strengthen the health system by integrating services at the community and facility levels. The study aims to provide a continuum of care from the community to referral facilities by addressing multiple types of MNH mortality, integrating MNH efforts with other health programs (e.g., HIV/AIDS, malaria, and nutrition), and linking actions at the regional, district, and community levels.

USAID is developing integrated packages of service that include AMTSL, ENC, and postpartum family planning to ensure that a continuum of care is being provided to both mother and child within programs. Studies in Mali and the Democratic Republic of the Congo are assessing the feasibility of an integrated package of services provided by CHWs, who are responsible for the majority of deliveries and could provide ENC and postpartum family planning services immediately after birth. Other USAID-supported research will examine the impact of integrating MNH interventions on access to services, quality of care, and the associated costs.

In order to promote comprehensive, integrated postnatal care delivered by skilled providers for mothers and their newborns, USAID is supporting a WHO systematic review of evidence to revise existing guidelines on the needs of the mother-infant dyad. In addition, a USAID-supported study will develop a model to enable programs to better target MNH interventions to those who are most vulnerable due to antenatal and postpartum complications such as low birthweight and maternal anemia. The study will assess the potential impact and feasibility of targeting strategies, their cost at scale, and barriers to implementation.

Child, Environmental, and Urban Health

Areas of Research and Introduction

Integrated Community Case Management of Childhood Illnesses

Pneumonia, diarrhea, and malaria account for 18 percent, 15 percent, and 8 percent of under-5 mortality, respectively; many of these deaths occur outside the health facility. In areas with limited access to health facilities, USAID-supported research has shown that community case management (CCM) is effective for the treatment of pneumonia. The next step is to move beyond demonstrating effective treatment for a single disease to implementing large-scale, countrywide community-based programs that effectively address the other causes of child death.

Studies have shown that many cases of pneumonia, diarrhea, and malaria can be managed safely and effectively by CHWs. USAID has been working on an approach to addressing program and policy barriers that involves limited treatment for nonsevere pneumonia and supports the integration of community approaches into the joint treatment of pneumonia, diarrhea, and malaria. This is accomplished with appropriately trained, equipped, and supervised health workers. This approach is known as integrated community case management (iCCM). Using case studies of countries that have taken this approach to scale, USAID is building the evidence base for iCCM to inform future implementation and scale-up.

Child, Environmental, and Urban Health Research Strategy 2006–2010

Total FY10: $2,168,000	
Strategy Themes	**Areas of Research and Introduction: Five-Year Strategy**
Integrated Community Case Management of Childhood Illnesses	Conduct demonstration studies in selected countries
	Conduct effectiveness studies on joint treatment with antibiotics and artemisinin-based combination therapy
Community Treatment of Severe Pneumonia	Conduct effectiveness studies of outpatient and community health worker treatment of severe pneumonia
Diarrhea Therapy and Prevention	Assess impact of inclusion of zinc into diarrhea treatment programs to reduce child morbidity and mortality
	Develop and support the implementation of effective use of zinc in diarrhea treatment programs
	Conduct catalytic studies to identify and address the factors increasing diarrhea mortality and oral rehydration therapy
Water Supply, Sanitation, and Hygiene	Develop scalable approaches to improve hygiene behavior and provide clean drinking water
Reduction of Indoor Air Pollution	Develop scalable approaches to reduce the impact of indoor air pollution on health
Urban Health	Assess the impact and effectiveness of community-based urban health programs

USAID supported a study in Rwanda on the efficacy of a newly introduced iCCM program. The study measured the utilization of CHWs and health facility services for sick children under 5 years of age in six districts. From January to September 2009, CHWs provided 50.2 percent of all malaria treatments, 54.8 percent of diarrhea treatments, and 48 percent of pneumonia treatments without changing overall rates of referral to facilities. These results indicate the demand for and significant use of community-level treatment services. In addition, study data showed that compared with overall diarrhea rates, the rate of utilization of diarrhea treatment was low and the number of episodes treated by CHWs and health facilities was less than 10 percent of the expected incidence. Thus, the data suggest a need to improve approaches to diarrhea treatment, awareness, and prevention. These findings are being used by the Ministry of Health to improve and scale up iCCM in Rwanda. Incidentally, another study in Senegal is evaluating best practices and bottlenecks within the iCCM program implementation process. By linking program implementation with operational research, these studies are identifying evidence-based solutions to iCCM challenges in the field.

Additional research will assess the start-up and recurrent costs associated with large-scale, national iCCM and develop a costing model that can be used to generate country-specific data. The results of this work will inform the development of policies and implementation strategies for the successful introduction and scale-up of iCCM programs.

In rural and remote settings with limited health infrastructure, rapid diagnostic tests (RDTs) can provide an accurate diagnosis for malaria, thereby reducing the misdiagnosis of pneumonia cases – as both pneumonia and malaria initially present with a high fever – and the unnecessary, costly use of artemisinin-based combination therapy (ACT), an antimalarial drug. A study in Zambia demonstrated the effectiveness and feasibility of CHWs in managing pneumonia and malaria with the aid of RDTs. CHWs without RDTs dispensed antimalarial medicine to 99 percent of all children they saw who had fevers, regardless of whether they actually had malaria. By contrast, only 28 percent of the children with fevers seen by CHWs with RDTs received antimalarial drugs, closely matching the number of children who actually had malaria. Findings from this study show that CHWs have the capacity to use RDTs, ACTs, and amoxicillin to manage malaria and pneumonia. The application of these findings can reduce overuse of ACT, cut down on drug and program costs, and provide children with early and appropriate treatment for pneumonia.

Severe Pneumonia Community-Based Treatment

USAID, in collaboration with the WHO, is undertaking a study in Pakistan to build the evidence base for CCM of severe pneumonia. The study is determining whether government CHWs, known as lady health workers, can improve care-seeking and management of severe pneumonia in the community by correctly assessing cases and providing appropriate treatment. If the findings prove the intervention to be effective and safe, they will be used to develop formal WHO guidelines for the promotion of CCM for severe pneumonia and to scale up pneumonia programs in Pakistan and other countries.

A USAID-supported study also is evaluating the effectiveness of antibiotic therapy for severe pneumonia among children under 5 in high-HIV-prevalent settings in sub-Saharan Africa. The study seeks to identify alternative treatment strategies for severe pneumonia among HIV-infected/HIV-exposed children under 5 and provide solid evidence to develop guidelines for these specific populations.

Diarrhea Management: A Return to Oral Rehydration Therapy

In 2004, WHO and UNICEF released a joint statement recommending zinc for the treatment of acute diarrhea along with oral rehydration therapy (ORT) and oral rehydration solution (ORS). USAID supported implementation studies and scale-up efforts to identify how to increase effectively the availability and uptake of zinc/ORT treatment in the public and private sectors.

A USAID-supported program in Benin demonstrated the effectiveness of building upon an existing ORS brand to launch a new branded diarrhea treatment kit that combined ORS and zinc treatments. At the end of the program, 31 percent of caregivers had used zinc to treat their child during an episode of diarrhea. Mass media combined with community-based interpersonal communication efforts were the main sources of information on ORS and zinc use, with radio spots being the primary source of information for families.

Results from a program in Nepal show the importance of mass media and public-private partnerships in improved diarrhea treatment efforts. Using a multichannel communications campaign that promoted ORS and zinc to public health professionals, private drug suppliers, and caregivers, knowledge and use of zinc increased from 4

to 15.4 percent in five months. Exposure to mass media messages was effective in improving zinc-related knowledge and was a significant predictor of correct zinc use.

USAID also supported a study that assessed programs to create supply and demand for zinc/ORS treatment in Tanzania. Private-sector involvement contributed significantly to the creation of a sustainable supply of quality zinc treatments produced by local manufacturers. Sufficient demand for zinc treatment was developed through a multichannel public-private partnership that promoted zinc/ORS to health professionals, drug suppliers, and caregivers. These studies highlight the importance of public-private sector involvement.

Water, Sanitation, and Hygiene

Diarrhea may be prevented by ensuring safe drinking water at household-level point of use using low-cost treatment products (both filter and consumable based). In India, a USAID-supported study is evaluating the efficacy and feasibility of using Aquatabs™ – water purification tablets that prevent waterborne diseases such as cholera and dysentery. The study also is evaluating the effects of Aquatab™ use on weight gain among children under 5, school absenteeism, and lost days at work to understand how this water sanitation intervention influences overall health and productivity. The study will determine whether Aquatabs™ are suitable for potential long-term use by measuring the product's acceptability and the extent to which it is used correctly and consistently by the study population.

USAID is supporting a review of the Total Sanitation and Sanitation Marketing program, which combines approaches that raise demand for community-led total sanitation with marketing of sanitation products and services. This research activity will build the body of knowledge around Total Sanitation and Sanitation Marketing approaches that USAID could use in developing sanitation programs at scale in maternal and child health priority countries.

Approximately 90 percent of people living with HIV/AIDS are affected by diarrhea related to unsafe water, inadequate sanitation, and poor hygiene. A USAID-supported study utilized the Trials of Improved Practices approach to identify feasible, incremental steps that move people toward improving practices in Ethiopia, Tanzania, Uganda, and Kenya. The study determined and validated desirable water, sanitation, and hygiene (WASH) practices in each country by negotiating small doable actions – behaviors that are considered feasible to the target group given their existing context and resources and have a personal and public health impact, even though they are not "ideal" practices. The household WASH practices identified were similar across the four countries, demonstrating that most small doable actions to integrate WASH into HIV/AIDS programs are the same in East Africa and probably across across the rest of the continent. Consequently, small doable actions can be confirmed in new country settings with minimal research and adapted as necessary.

Indoor Air Pollution

Acute respiratory infections annually kill an estimated 2 million children under the age of 5; about 800,000 of those deaths are associated with high levels of indoor air pollution caused by indoor cooking with biomass fuels by the rural and urban poor. USAID is supporting research to develop evidence-based interventions and approaches that will reduce this risk, including qualitative research on incentives for the purchase and use of improved cook stoves as well as market-based strategies to reach high-risk populations.

Urban Health

A study in India developed and tested the effectiveness of approaches to delivering coordinated, cost-effective and scalable maternal, newborn, and child health (MNCH) services among the urban poor. Initial assessment on the availability, coverage, and quality of MNCH services within 11 urban slums found practices to be at suboptimal levels, with 72 percent home births and 7 percent skilled birth attendance; a 10 and 22 percent use of thermal and clean cord care practices, respectively; and a 51 percent timely initiation of breastfeeding. The study evaluated the effectiveness of two interventions for improving behaviors at the household level and generating demand for, and increasing utilization of, services: the demand-supply linkage approach and the ward coordination approach. Both approaches led to improvements in MNCH, such as the doubling of complete immunization rates among 1 year olds. The demand-supply linkage model required more resources, while the ward coordination approach expanded the supply of services without effectively generating demand. These findings will be used to further the development of effective urban health interventions and inform policies that target urban slums.

A study in Ethiopia is assessing the efficacy and productivity of urban-based CHWs in order to inform the development and scale-up of programs in the country. USAID is also supporting the development of appropriate metrics for measuring community-based MNCH in urban settings. As poor sanitation is a key contributor

Child Survival and Health Grants Program Planned Research Activities

Country	Research Description
Bangladesh	Determine the extent to which a community mobilization model to build and institutionalize community engagement in health is more successful and/or cost-effective in reaching poor and marginalized mothers and newborns than existing government programs
Nepal	Assess the implementation of home-based newborn care, with additional health facility improvements and community-facility linkages, to demonstrate that integrated approaches can amplify intervention impact on maternal and newborn health
Ecuador	Assess the implementation of early home-based postpartum care by ambulatory health teams and traditional birth attendants to coordinate a continuum of MCH services from home to facility and improve maternal and newborn health
Zambia	Determine the feasibility and effectiveness of an integrated CHW-traditional birth attendant teams trained on the community-based delivery and use of treatments for infections (i.e., iCCM) among children 0–59 months of age
Honduras	Assess the extent to which implementation of standardized community-based MNCH interventions by community health volunteers in hard-to-reach areas improve health care demand, access, and quality at improved cost, when compared with a facility-based system
Niger	Determine the feasibility, effectiveness, and cost of introducing treatments for infections (i.e., iCCM) of children 0–59 months of age provided by select, trained semiliterate mothers versus provision of care exclusively through health facilities

to ill health in urban settings, studies in Bangladesh and India are examining ways to integrate handwashing into urban essential newborn care activities.

Child Survival and Health Grants Program

USAID's Child Survival and Health Grants Program (CSHGP) supports U.S. private and voluntary organizations (PVOs), nongovernmental organizations (NGOs), and their local partners to leverage "what works" in community-oriented programming and to implement innovative and effective MNCH nutrition and infectious-disease projects that reduce morbidity and mortality.

The CSHGP places a strategic emphasis on operations research (OR), encouraging PVOs to test and evaluate interventions that address local challenges, improve local health program implementation and use of data, spur national policy dialogue, and ultimately strengthen sustainable national programs. Grantees receive technical assistance from USAID's flagship Maternal and Child Health Integrated Program to build PVO/NGO capacity in designing and implementing OR.

Country-level examples of research by CSHGP grantees and their local partners include:

- Trials of chlorhexidine (CHX) lotion applied to newborn umbilical stumps, which have shown great promise in reducing neonatal sepsis and mortality among newborns in health facility settings in Nepal. A study in Nepal is assessing the uptake and proper application of CHX by birth attendants as well as the coverage and costs of two potential delivery channels for CHX: (1) distribution outlets such as health facilities and pharmacies; and (2) community health providers, including female community health volunteers and auxiliary nurse midwives. If proven successful in the community (i.e., correct and consistent use by birth attendants), CHX lotion may be recommended for use in both institutional and home births in Nepal's national neonatal health strategy.

- An evaluation of the impact of an innovative agriculture and nutrition programming model that combines homestead food production, which includes implementation of home gardens and small animal husbandry, with behavior change communications strategies to promote the adoption of Essential Nutrition Actions[1] to improve household food security, diet quality, and nutrition outcomes. The study, ongoing in Nepal, will determine whether this integrated agriculture-health

1 The seven essential nutrition actions are (1) optimal breastfeeding during the first six months, (2) optimal complementary feeding from age 6 months and up, (3) nutritional care of the sick and severely malnourished child, (4) prevention of anemia, vitamin A deficiency, (5) adequate intake of iron and folic acid and prevention of anemia, (6) adequate intake of iodine, and (7) optimal nutrition for women.

promotion model can significantly improve nutrition among children 12–48 months of age. This research has the potential to provide evidence in support for intersectoral programming across both agriculture and health sectors to address child undernutrition, food security, and health.

- In Mozambique, a study explored the feasibility and effectiveness of community-based delivery of zinc/ORS treatments by CHWs for the management of childhood diarrhea. Building on an examination of the key challenges affecting the treatment of diarrhea in children, 108 CHWs were trained to assess, treat, and counsel families on childhood illnesses. Over a six-month period, 5,416 children under 5 were treated with zinc/ORS: 2,868 in health facilities and 2,548 within the community. Currently, the Ministry of Health (MOH) is preparing an operational plan for a revitalized role of the CHW that likely will include management of common childhood illnesses. These study findings will inform the development of a national diarrhea treatment protocol that may be scaled up.

- Six awards made in 2009 have enabled the carrying out of OR that contributes to national health systems strengthening by bringing health interventions and trained providers closer to communities, institutionalizing civil society engagement in health, training CHWs, and improving health facility-community linkages. Along with the MOH, PVO grantees have developed OR concepts based on local challenges and information gaps in order to facilitate research utilization and uptake of successful programmatic innovations in-country. Partnerships forged by PVO grantees and local and U.S. universities and research institutions will leverage and/or continue to build expertise in health OR and facilitate strategic dissemination of results.

Key Partners in Child, Environmental, and Urban Health Research and Introduction

Boston University

ChildFund International

Christian Reformed World Relief Committee

Concern Worldwide

Food for the Hungry

HealthRight International

Helen Keller International

International Centre for Diarrhoeal Disease Research, Bangladesh

John Snow, Inc.

Ministry of Health (Mozambique)

Ministry of Health and Population (Nepal)

Mother and Infant Research Activities (Nepal)

National Institute of Statistics (Mozambique)

Nepali Technical Assistance Group

Plan USA

Save the Children

University Research Co., LLC, Center for Human Services

USAID/Mozambique

USAID/Nepal

Nutrition

Issues and Rationale

Undernutrition affects nearly 200 million children worldwide and contributes to more than 3.5 million child deaths each year. More than one-third of children in the developing world are undernourished, and 2 billion people suffer from micronutrient deficiencies. Improving nutrition is critical for MCH outcomes, a driver of economic growth and poverty reduction, and central to development. Nutrition is the integral intersection of the Feed the Future and the Global Health Initiative that share the same objective of reducing undernutrition by 30 percent in priority countries through integrated program approaches.

USAID supports research to improve the design and delivery of food and nutrition interventions that target the most vulnerable populations. This includes a focus on vitamin A deficiency prevention and control, anemia prevention and treatment, Community-based Management of Acute Malnutrition (CMAM), and dietary quality and diversity.

Areas of Research and Introduction

Vitamin A Deficiency – Prevention and Control

More than 130 million children and 7 million pregnant women suffer from vitamin A deficiency, which can lead to negative health consequences, including increased morbidity, mortality, and childhood blindness. Recently, USAID-supported research in Bangladesh documented that vitamin A given to a newborn in the first 48–72 hours of life reduces infant mortality by 20 percent in vitamin A-deficient populations. Based on results gathered in Bangladesh as well as in Nepal, the Agency

Nutrition Research Strategy 2006–2010

Total FY10: $4,100,000	
Strategy Themes	**Areas of Research and Introduction: Five-Year Strategy**
Vitamin A: Deficiency Prevention and Control	Establish effectiveness of newborn dosing in Asia to reduce infant mortality and delivery approaches in an effective and cost-effective manner
	Establish effectiveness of maternal vitamin A supplementation in reducing maternal mortality
Iron: Anemia Prevention and Treatment Packages	Organize WHO/UNICEF consultation on safe delivery of iron to deficient children in order to provide programmatic guidance to countries and to identify and undertake priority research as appropriate
	Establish best practices for the increased coverage and implementation of reproductive health packages, which include anemia control and prevention
	Determine the constraints to anemia control and develop programmatic options to overcome them
Dietary Quality and Diversity	Assess impact of micronutrient powders on treating anemia and other micronutrient deficiencies
	Improve the measurement of dietary quality and diversity
	Prevent and cure undernutrition through use of lipid-based nutrient supplements
Community-based Management of Acute Malnutrition	Implement developed and accepted WHO guidelines for community therapeutic care and home-based care in five countries
	Assess and identify suitable locations and institutions for local production of ready-to-use therapeutic foods
	Test alternative formulations of ready-to-use therapeutic foods for cost and local effectiveness

Spotlight: Advances in Measuring Dietary Quality and Diversity

USAID has supported the development and validation of three new tools to better monitor and evaluate dietary quality and diversity of infants, young children, and women, as well as household hunger. These innovative and simplified measurement tools have been adopted by the Feed the Future initiative and the Global Health Initiative to improve the planning, design, and monitoring systems of USAID-supported nutrition activities.

1. Indicators for Assessing Infant and Young Child Feeding Practices: Indicators for Assessing Infant and Young Child Feeding practices directly affect the nutritional status of children during the critical window of opportunity and ultimately have an impact on child survival. However, current indicators focus mainly on breastfeeding, and the lack of consensus on indicators to measure feeding practices has been an obstacle to measuring and improving infant and young child nutritional outcomes. New simple, valid, and reliable indicators have been developed following a five-year effort and include a focus on food-related aspects of child feeding that will be used to improve assessment, targeting, and monitoring and evaluation activities.

2. Women's Dietary Diversity: Women of reproductive age are among those most likely to suffer from micronutrient deficiencies, yet in developing countries there is limited data on the quality of women's diets and their micronutrient status. Results from Bangladesh, Burkina Faso, Mali, Mozambique, and the Philippines indicate that food-group diversity indicators are very promising and may be a simple and valid option for population-level assessment and for monitoring progress toward improved micronutrient intakes among women of reproductive age.

3. Household Hunger Scale: Separate indicators and data collection methods are needed to assess each of the three elements underlying food security attainment. However, cross-culturally equivalent methods for assessing the access component either are unavailable or lack field practicality. Household hunger scale provides a useful method for assessing household hunger cross-culturally, using a validated and field-practical approach. Household hunger scale can help to advance evidence-based research to improve food security and household hunger globally while also strengthening the ability of governments and international and national agencies to advocate for policies and programs to prevent and address household hunger.

is extending this research to the operational challenges and cost of distributing vitamin A to newborns. These findings will be the basis for national programs in newborn vitamin A supplementation. Notably, the WHO and other partners are taking this research to other countries to assess the intervention's impact in order to enable a global recommendation.

Iron – Anemia Prevention and Treatment Package

Anemia affects one in four people globally, nearly half of all preschool-age children, and more than 40 percent of all pregnant women. Anemia contributes to 20 percent of all maternal deaths and has long-term negative effects on cognitive function, work productivity, and economic growth. Iron deficiency is one of the major causes of anemia, which can be prevented with evidence-based prevention and treatment packages. However, the clinical diagnosis of anemia and the scale-up of service delivery, including drug management, have been major obstacles to the diagnosis and treatment of anemia in women and children.

In order to better diagnose and understand the causes of anemia, USAID is supporting the development of a portable device to rapidly test for anemia and identify specific underlying causes of the condition. This device would determine hemoglobin levels, measure iron status, and detect the presence of infectious diseases commonly associated with anemia, such as malaria and helminthes.

To improve access to health services and improve drug supply and management, USAID funded assessments in Cambodia, India, and Uganda that measured the overall prevalence of anemia and guided plans for scale-up of anemia prevention and treatment services. In the state of Jharkhand in India, the findings prompted the Ministry of Health to make two major policy changes: (1) the modification of its objective on maternal anemia, resulting in an increase in the proportion of women receiving iron folic acid supplements from 32 percent to 69 percent; and (2) the integration of deworming into anemia prevention services for pregnant women. In Uganda, assessment results have led to the development of comprehensive maternal anemia guidelines that will be used by service providers.

Dietary Quality and Diversity

USAID is supporting research on food-based approaches to improve dietary quality and diversity, including improving program effectiveness research to validate the

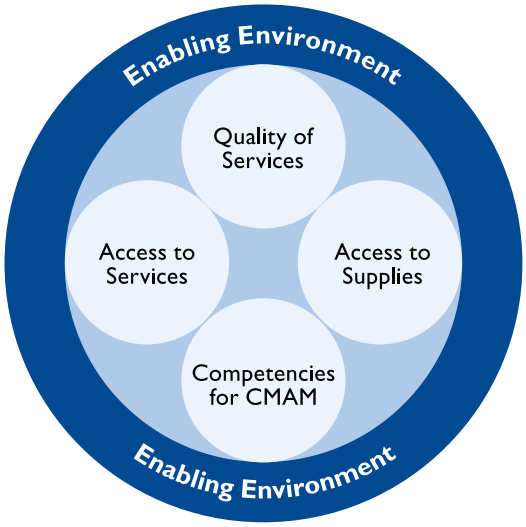
measurement of dietary quality and diversity; assess the impact of micronutrient powders on anemia and other micronutrient deficiencies; and prevent and treat undernutrition with lipid-based nutrient supplements.

Studies in Burundi and Guatemala are assessing cost-effective models for the Prevention of Malnutrition in Under 2s Approach (PM2A). PM2A is a package of interventions aimed at preventing child undernutrition by addressing the key underlying determinants of undernutrition, including access to sufficient food, being in good health, and receiving adequate feeding and care. In Guatemala, the study is assessing optimal sizes of rations for PM2A participants, determining the potential role of new food products in a PM2A context as well as the optimal timing and duration of exposure to PM2A that have the highest nutritional impacts on women and children.

Lipid-based nutrient supplements are a range of nutrient-dense products in which vitamins and minerals are added to a lipid-based product that is added to foods for consumption. The products are generally composed of a vitamin-mineral mix combined with vegetable fat, peanut paste/soy, dried milk or whey, and sugar. USAID-supported research has shown nutrient-dense products, such as Plumpy'nut® or other ready-to-use therapeutic foods (RUTFs) to be very effective in small- and large-scale programs for the treatment of severe acute malnutrition (SAM). Based on the success of RUTF in the treatment of SAM, additional lipid-based nutrient supplements have been developed for the prevention of undernutrition. Efficacy trials involving administration of these lipid-based nutritients to prevent severe stunting in children over 6 months of age documented linear growth of children, reduce iron deficiency anemia, and enhance motor development. The reversal of stunting in young children by lipid-based nutrient supplement products has been a significant advance in the use of food to improve dietary quality. In order to better understand the performance of lipid-based nutrient supplements and micronutrient powders when provided in a programmatic setting, USAID is supporting effectiveness studies to determine the best program options to prevent undernutrition in Bangladesh and Guatemala.

Biofortification of commonly eaten foods and staples is another approach that can contribute to dietary quality and diversity. USAID-funded research has shown that increasing the bioavailability of limiting nutrients – such as vitamin A, iron, and zinc – in staple food crops, including beans, rice, maize, cassava, and sweet potatoes, can improve the consumption of a diverse diet and lead to improved nutritional status. USAID and other donors

Figure 1. Key Domains for Integration of Community-Based Management of Acute Malnutrition



supported research on a newly developed biofortified maize that showed an 18-fold increase in beta-carotene content, which the body can convert into vitamin A. While research currently is focused on the development of new biofortified crops, additional studies will be undertaken to develop and implement plans for the production and consumption of these crops by the most vulnerable. The success of the biofortified sweet potato is being repeated in crops that represent the major sources of energy, protein, and micronutrients.

Community-Based Management of Acute Malnutrition

Acute undernutrition contributes to the death of more than 1 million children every year. Community-based Management of Acute Malnutrition (CMAM), an approach pioneered by USAID and NGO partners, detects acutely undernourished children; provides RUTF at the community level; and strengthens referral systems to treat those with complications at medical facilities.

A three-country study in Ethiopia, Malawi, and Niger identified key domains that contribute to the successful integration of CMAM into national health systems (Figure 1). Information from this assessment has supported the integration of CMAM into national health systems and facilities in Ghana, Sudan, and South Sudan. An assessment of CMAM implementation in Burkina Faso, Mali, and Mauritania is identifying challenges, opportunities, gaps, and lessons learned in implementation,

building on regional and global work in this area. Further studies are needed to refine the factors and processes that influence the quality of integration to guide integration and scale-up.

RUTFs are an integral part of the success of the CMAM approach. Clinical effectiveness studies in Malawi are identifying improved formulations of RUTF for use in CMAM programs. One study found use of a 20-percent-lower-cost product (10-percent-milk RUTF) resulted in a lower rate of recovery and slower growth rates when compared with the standard 25-percent-milk RUTF. A separate study in Malawi is assessing relative rates of recovery for children ages 6–59 months with moderate acute malnutrition, using an improved milk-fortified corn soy blend developed by the World Food Programme and two RUTFs – a soy-peanut-fortified spread and Supplementary Plumpy®. The results of both studies will contribute to improved global standards for CMAM and their eventual scale-up in partner countries.

Research is assessing whether mid-upper arm circumference measures may be used safely as a program discharge criterion for CMAM without increasing risk of mortality. This has the potential to allow CMAM services to be delivered at peripheral health facilities by CHW programs, and in resource-scarce settings, where the use of the weight-for-height measure is problematic. In addition, a study in Malawi is testing whether there continues to be a need for antibiotics to treat SAM without medical complications in outpatient-based settings. The results of this work would help simplify outpatient SAM treatment within CMAM by eliminating the requirement for presumptive treatment with antibiotics.

Key Partners in Nutrition Research and Introduction

Academy for Educational Development
Bill & Melinda Gates Foundation
Canadian International Development Agency
Concern Worldwide
Global Alliance for Improved Nutrition
ICDDR,B (Bangladesh)
International Food Policy Research Institute
Johns Hopkins University
Management Sciences for Health
Micronutrient Initiative
National Institutes of Health
Partner government ministries of health
PATH
Save the Children
Tufts University
UNICEF
University of California at Davis
University of Malawi
University Research Co., LLC
U.S. Pharmacopeia Drug Quality and Information Program
Valid International
Washington University in St. Louis
World Bank
World Food Programme
World Health Organization

Family Planning and Reproductive Health

Issues and Rationale

Enabling couples to determine whether, when, and how often to have children through family planning (FP) services is vital to safe motherhood and healthy families. FP reduces unintended pregnancy, which consequently reduces abortion, maternal and child mortality, and HIV/AIDS infection. It is estimated that FP alone can prevent 25 percent of maternal and child deaths in developing countries; thus, the availability of a wide range of contraceptive choices can ultimately promote maternal health and child survival. However, more than 64 million women in developing countries who would like to use contraception to postpone pregnancy are not using it, and in sub-Saharan Africa, 75 percent of the population does not have access to a minimal range of contraceptive options. In addition to this unmet need for contraceptives, nearly every developing country needs substantial improvements in the quality of existing FP services and effective ways to reach out to youth, men, and other vulnerable populations.

USAID-led family planning and reproductive health (FP/RH) research includes biomedical, operations, demographic, evaluation, applied, and social science research. The primary aim of FP/RH research is to develop, test, introduce, and scale up new and improved technologies, tools, and approaches to decrease unintended pregnancies and prevent the transmission of HIV and other sexually transmitted infections (STIs) in developing countries.

Areas of Research and Introduction

Contraceptive Research and Development

USAID's contraceptive research and development (R&D) program aims to improve RH and expand FP use through the provision of a wide range of new and improved

Family Planning and Reproductive Health Research Strategy 2006–2010

Total FY10 : $23,335,000	
Strategy Themes	**Areas of Research and Introduction: Five-Year Strategy**
Contraceptive Research	Improve and expand the range of barrier methods
	Develop and improve fertility awareness-based methods
	Develop long-acting hormonal methods in novel delivery systems
	Develop and improve other long-acting and permanent methods
Improving and Expanding the Use of Contraceptive Methods and Services	Improve the use of barrier methods to reduce unintended pregnancy and the transmission of sexually transmitted infections
	Improve the use of hormonal methods by expanding access
	Improve and expand the use of fertility awareness-based methods
	Expand the distribution of, and access to, long-acting and permanent methods
Improving Approaches to Address Unmet Need for Family Planning Services of Underserved Groups	Improve approaches to reach postpartum women, the urban poor, and men
	Determine effective and appropriate programs to improve the reproductive health of youth
	Identify effective models to provide family planning safely through rural community networks, especially in Africa
Improving Integration of Family Planning and Other Health Care Services	Improve the integration of family planning into maternal and child health, HIV, and other health services
	Assess cost efficiency of integrated services

Spotlight: Mobile Phone-Based Family Planning and Reproductive Health Program

USAID-supported feasibility research was conducted on the use of text messaging for FP services within a mobile phone-based FP/RH program (Mobile4RH). Stakeholders in Tanzania and Kenya, including the MOH, directors of private sector clinics, the United Nations Population Fund, and other collaborating agencies, found the idea to be acceptable and feasible. Results showed that the clients liked the privacy of the service, use of the mobile phone as a method of communicating FP information, and the reiteration of messages initially received in a clinical setting. As a result, USAID is moving ahead with the development and launch of this text messaging service in Tanzania and Kenya and is working with the Division of Reproductive Health in Nairobi, Kenya, on a mobile phone FP provider notification system that will be linked with continuing medical education credits for providers.

contraceptive methods that are affordable, acceptable, and easy to apply within low-resource settings.

Advances in Contraceptive R&D

A USAID-supported clinical trial tested the effectiveness, safety, and acceptability of the Nestorone®/Ethinyl Estradiol contraceptive vaginal ring, a female-controlled hormonal method that lasts for up to 12 months. Preliminary results indicated that the product (1) is 87.5 percent effective in preventing pregnancy when used according to instructions; (2) produces favorable bleeding patterns as reported by clients; (3) provides a rapid return to fertility for those seeking to become pregnant after use, reaching about 80 percent in six months; and (4) has an estimated 80 percent user satisfaction. The safety precautions and warnings for the Nestorone®/Ethinyl Estradiol contraceptive vaginal ring are consistent with currently available combined hormonal contraceptives. These results support USAID's continued efforts to develop a user-controlled, long-acting contraceptive that does not require daily attention from women or the availability of trained health providers for insertion or removal. This one-year contraceptive method can also potentially fill the FP method gap between the three-month injectable and the five-year implant FP methods, thereby expanding individualized FP choices for women.

USAID is supporting a large-scale contraceptive effectiveness and safety study of the SILCS diaphragm, a "one-size-fits-most" reusable barrier method. Preliminary results demonstrated that SILCS is just as effective as the standard diaphragm. Once approved by the U.S. Food and Drug Administration for contraceptive use, additional studies will be undertaken to determine the effectiveness of the SILCS diaphragm in preventing STI transmission. USAID also is supporting a safety study of another barrier method, known as the woman's condom, concurrently with a Eunice Kennedy Shriver National Institute of Child Health and Human Development contraceptive effectiveness trial for the device – an excellent example of leveraging and cost efficiency among U.S. Government agencies.

A separate study measuring the long-term effectiveness of the Two-Day Method™ – a simple fertility awareness-based approach – among women in several developing country settings found Two-Day Method™ to have an average effectiveness of 88 to 96 percent, depending on correct use. Method continuation was also high, averaging 61 percent after three years of use. Such results strengthen the evidence for the sustainability and cost-effectiveness of this approach.

In India, a clinical study is assessing the effectiveness of three different vasectomy techniques. Results from this trial will inform programs and the Ministry of Health (MOH) on best practices and methods to improve interventions that utilize vasectomy as a method of FP.

USAID research aims to increase understanding about the safety and effectiveness of contraceptive use among women at high risk of HIV infection and women who are undergoing antiretroviral therapy (ART). A clinical trial of HIV-positive women suggested that ART use does not change the effectiveness of the injectable contraceptive Depo-Provera, one of the most popular hormonal contraceptives. USAID is supporting similar studies to assess the impact of ART on combined oral contraceptives and hormonal implants.

USAID is also supporting research to develop the Depo-Provera/Uniject™ device. Uniject™ is a single-use syringe that can be prefilled with Depo-Provera and administered with minimal training. This device has the potential to increase access significantly to FP by expanding services into hard-to-reach areas through distribution by community health workers (CHWs). In collaboration with the WHO, the Agency also convened a meeting on addressing policy barriers to contraceptive use.

Advances in Improving and Expanding the Use of Contraceptive Methods and Services

Previous USAID-supported studies in developing countries have demonstrated the effectiveness of the Standard Days Method (SDM) within FP programs (96 percent

effective). SDM is a simple fertility awareness-based method that teaches couples to recognize when they are most fertile and informs them on how to avoid unprotected sex during these periods. A USAID-supported assessment of current SDM programs showed that the method can be taught effectively at all levels of the health system, through community workers and non-health workers, including agricultural cooperative members, and through novel distance-learning approaches. These findings will be used to accelerate the scale-up of this approach in FP programs.

In India, Rwanda, and Peru, evaluation and impact studies showed that SDM also improves couple communication, brings new users into the health system, and increases overall contraceptive prevalence. The method has been introduced in more than 25 countries through both FP/RH and maternal and child health (MCH) services in the public and private sectors and currently is being scaled up in several countries, including Rwanda, the Democratic Republic of the Congo, India, Mali, Guatemala, and Kenya.

Studies have shown that training community-based nurses to provide the intrauterine device (IUD) is feasible and acceptable and shows promise for increasing use of long-acting and permanent contraception methods (LAPMs). In Ghana, a USAID-supported study assessed a community-based FP/RH program that provided a range of contraceptive methods. Results pointed to a general increase in LAPM awareness as well as an increase in the proportion of FP users choosing IUDs. Another study in India demonstrated that a package of interventions designed to increase awareness and availability of the IUD significantly increased its use in both urban and rural settings. The materials developed for the project are now being adapted for use on a national scale by the Indian Government.

USAID studies of community-based distribution of injectable contraceptive programs in Uganda and Madagascar confirmed results from earlier similar studies that community-level workers are indeed able to provide Depo-Provera as safely and effectively as clinically trained providers, thus significantly increasing access to this popular method. Results of these studies are being used to scale up the provision of this method at the community level in several countries in sub-Saharan Africa and develop new tools for injectables (such as Depo-Provera/Uniject™).

Key Partners in Family Planning and Reproductive Health Research and Introduction

CONRAD

Department of Health and Family Welfare (India)

Division of Reproductive Health (Kenya)

Eunice Kennedy Shriver National Institute of Child Health and Human Development

Family Health International

Georgetown University, Institute for Reproductive Health

Health and Family Welfare Centers (Bangladesh)

IntraHealth International

Jhpiego

Management Sciences for Health

Meridian Group International, Inc.

PATH

Pathfinder International

Pfizer

Population Council

Save the Children

Schering AG

UNFPA

U.S. Centers for Disease Control and Prevention

U.S. President's Emergency Plan for AIDS Relief

World Health Organization

Family Planning Operations Research

Through operations research (OR), USAID aims to improve the availability and effectiveness of FP and integrated RH programs in developing countries. OR activities allow the Agency to respond promptly to requests and feedback from FP programs in the field, design culturally appropriate programs and service delivery approaches to address identified gaps, develop tools and materials to improve provider performance, scale up evidence-based practices, and improve the capacity for behavior change communications (BCC) to increase client awareness and use of existing services.

Advances in Improving Family Planning Services for Underserved Groups

In societies characterized by early marriage, most adolescent girls' first sexual experiences and needs for RH-HIV

services are within marriage. As such, these young women tend to fall within the gap that exists between conventional programming for adolescents and adults. USAID is supporting studies in Ethiopia and Kenya to test the feasibility of reaching the underserved population of married adolescents through faith-based structures. These studies developed strategies to educate newly married girls and their families about their RH-HIV vulnerability, empower them through membership in peer support groups, and facilitate access to relevant RH-HIV services. Working primarily through community-level faith-based structures in both countries, the studies have so far demonstrated both the tremendous need for such strategies and the feasibility of their implementation when such institutions are engaged.

Working with the Department of Health and Family Welfare in India, a USAID study demonstrated that BCC by CHWs increased use of postpartum FP methods, specifically the Lactational Amenorrhea Method (LAM).[1] The study developed and tested a BCC model that trained CHWs and used a community education campaign to increase use of LAM and later transition to other contraceptive methods. At four months, 20 percent of women were using LAM in the experimental sites, whereas no women were using LAM in the control sites. At nine months, the proportion using contraception in the experimental sites (63 percent) was double the control sites (32 percent); moreover, only 10 percent of women in the experimental sites were pregnant, compared with 16 percent in the control sites.

Advances in Improving Integration of Family Planning and Other Health Care Services

During the last five years, USAID has supported the development and testing of multiple approaches and models to integrate FP/RH with MCH services as well as different types of HIV services, including voluntary counseling and testing, prevention of mother-to-child transmission (PMTCT) of HIV, and home-based care, in order to increase the coverage and efficiency of FP programs.

In Kenya, USAID supported a study to evaluate an intervention that integrated FP with HIV care and treatment. The intervention centered on training providers in comprehensive HIV care centers and giving them the tools to provide FP services. The frequency of modern-method use among the clients of these centers increased to 52 percent from 36 percent before the intervention. Condom use also increased to 21 percent from 8 percent. These results have been used to develop Kenya's new national strategy for integrating FP-HIV services.

Table 1. Number of HIV-positive Births Averted by Current Contraceptive Use, by PEPFAR Country

PEPFAR Country	Annual no. of unintended HIV+ births currently averted by contraception
South Africa	120,256
Mozambique	18,395
Kenya	14,589
Zambia	12,823
Nigeria	12,434
Tanzania	11,975
Vietnam	8,827
Uganda	7,573
Botswana	4,172
Namibia	3,092
Ethiopia	2,728
Côte d'Ivoire	1,947
Haiti	912
Rwanda	561
Guyana	178

Source: Reynolds, H.W., Janowitz, B., Wilcher, R., and Cates, W. (2008) Contraception to prevent HIV-positive births: Current contribution and potential cost savings in PEPFAR countries. *Sex Transm Infect*, 84(Suppl II), ii49–ii53. DOI:10.1136/sti.2008.030049.

A USAID-supported analysis of data from the 15 U.S. President's Emergency Plan for AIDS Relief (PEPFAR) focus countries found that contraceptive use prevents hundreds of thousands of HIV-positive births each year by preventing unintended pregnancies in infected women (Table 1).

USAID supported a study that presented an overview of early integration efforts of FP with voluntary counseling and testing and HIV care and treatment services in five countries: Ethiopia, Kenya, Rwanda, South Africa, and Uganda. Separate evaluations of PMTCT services were also carried out in Kenya, Rwanda, and South Africa. All studies documented a high unmet need for FP among HIV clients. The studies found favorable policy environments for integration as well; however, they also found many obstacles to successful integration at the service-delivery level, such as training, supplies, and funding streams.

1 The Lactational Amenorrhea Method (LAM) is a modern, temporary contraceptive method based on natural infertility resulting from certain patterns of breastfeeding. Because LAM is a short-term, temporary contraceptive method, an essential component of LAM services is the timely introduction and ongoing use of another contraceptive method.

HIV/AIDS

Areas of Research and Introduction: Five-Year Strategy 2006–2010	FY 2010 Funding
Vaccines	$28,710,000
Microbicides	$45,000,000
Applied Research and Public Health Evaluation	$4,625,000

Issues and Rationale

Worldwide, an estimated 33 million people are living with HIV; 22 million of these individuals live in sub-Saharan Africa alone. Women are at increased risk, making up more than half of all global cases of HIV/AIDS, and 60 percent of the cases in sub-Saharan Africa.

Despite their great risk, many women in developing countries have difficulty protecting themselves from HIV infection through conventional prevention methods such as negotiating delay of sexual debut, partner reduction, and condom use, indicating that no single approach to HIV/AIDS prevention is likely to have a dramatic impact. Integrated approaches to prevention, detection, and management that are tailored to a specific country context and populations at risk yield the best results. Novel tools to prevent new HIV infections could complement currently available methods.

Areas of Research and Introduction

USAID supports innovative biomedical research to develop and introduce new products and technologies, such as vaccines and microbicides, to prevent HIV transmission, thereby mitigating the burden of HIV/AIDS in developing countries. USAID also supports applied and operations research while conducting public health evaluations to improve HIV/AIDS intervention programs, optimize program outcomes, and evaluate program impact.

Microbicides

Microbicides are a class of health products that can create an effective chemical barrier to sexually transmitted infections (STIs) and can be used to address the urgent yet unmet need for protecting women against HIV/AIDS. USAID is a global leader in microbicide

Spotlight: Advancing HIV Prevention Strategies for Women

In many countries, women lack the power to negotiate the use of prevention tools and approaches to protect themselves against HIV – in sub-Saharan Africa, women alone account for 60 percent of HIV infections. Therefore, a need exists for prevention methods that enable women to have greater control over HIV prevention. For more than one decade, USAID has been a global leader in the development of microbicides – products that can be applied vaginally to prevent sexual transmission of HIV – as one of several methods to address this urgent yet unmet need for women around the world.

In 2010, the U.S. Agency for International Development (USAID)-supported Center for the AIDS Program of Research in South Africa (CAPRISA) 004 trial in South Africa provided the first-ever proof that a microbicide, Tenofovir 1-percent vaginal gel can safely and effectively protect women from HIV transmission. The trial compared the use of Tenofovir 1-percent vaginal gel versus a placebo gel in 889 women at high risk of HIV infection, and Tenofovir 1-percent vaginal gel was shown to be 39 percent effective in reducing a woman's risk of acquiring HIV; effectiveness increased to 54 percent among women who used the product very consistently. Tenofovir 1-percent vaginal gel also was found to be 51 percent effective in preventing genital herpes infections in these women. If these significant protective effects are confirmed in further studies, widespread use of Tenofovir 1-percent vaginal gel at this level of protection could prevent more than one-half million new HIV infections in South Africa alone over the next decade.

USAID will continue to work with the U.S President's Emergency Plan for AIDS Relief, multilateral agencies, and partner countries to ensure this breakthrough in HIV prevention, and the full impact of its effects, can be offered to vulnerable women and girls worldwide, especially in low-resource settings.

Microbicides Research Strategy 2006–2010

Total FY10: $45,000,000	
	Areas of Research and Introduction: Five-Year Strategy
2006	Continue Phase III large-scale clinical effectiveness trials initiated FY 2004 and FY 2005 Identify new clinical trial sites for Ushercell™ and Savvy™ to begin in Africa and India Continue next-generation microbicide research/capacity building for future trials
2007	Continue Phase III trials: Carraguard™, Ushercell™, and Savvy™ Continue Phase IIB/III trials: Tenofovir 1-percent vaginal gel and oral Truvada in women Address policy and logistical issues for successful introduction into countries Pursue transfer of manufacturing capacity to developing country sites
2008	End Ushercell™ and Savvy™ trials as per Data Safety Monitoring Board Conduct Phase IIB/III trials: Tenofovir 1-percent vaginal gel and oral Truvada in women Assess final results of Carraguard™ trial Continue to address policy and logistical issues for introduction Continue to transfer manufacturing capacity
2009	Continue Phase IIB/III trials: Tenofovir 1-percent vaginal gel and oral Truvada in women Continue to address policy and logistical issues for introduction Continue to transfer manufacturing capacity
2010	Continue Phase IIB/III trials: Tenofovir 1-percent vaginal gel and oral Truvada in women Continue to address policy and logistics for introduction: procurement and financing distribution networks within public and private sectors, health delivery systems, information needs, and licensing Determine potential need for additional trials

R&D and remains committed to supporting the development of safe, effective, acceptable, and affordable microbicide products that are suitable for use in developing-country public sector programs. As such, USAID's activities include:

- Conducting research on preclinical microbicide product development and evaluation
- Developing and assessing safe and acceptable microbicide formulations and modes of delivery
- Carrying out clinical studies of potential microbicide products for safety, effectiveness, and acceptability
- Conducting relevant behavioral research

USAID's role in microbicide development is coordinated through extensive representation in and collaboration with the efforts of other U.S. Government agencies, as outlined in the 2006 *Report to Congress: Health-Related Research and Development Activities at USAID*.

Since early 2004, USAID had moved five promising microbicide candidates – Carraguard™, Ushercell™ (cellulose sulfate), Savvy™ (C31G), Tenofovir 1-percent vaginal gel, and oral Truvada – into the final stages of clinical testing in international trials for their safety, effectiveness, and acceptability in reducing the risk of HIV transmission, as indicated in the table "Areas of Research and Introduction: Five-Year Strategy." Trials for Savvy™ and Ushercell™ were ended, respectively, because completion at the sites chosen became futile and because safety concerns became apparent only in the larger trial.

Carraguard™ was found to be safe and acceptable, but it did not significantly prevent HIV infection.

In 2010, USAID made a historic breakthrough: Results from the CAPRISA 004 trial provided the first-ever proof that a microbicide, Tenofovir 1-percent vaginal gel, could safely and effectively reduce women's risk of HIV infection, as further described above in "Spotlight: Advancing HIV Prevention Strategies for Women." Once these results are confirmed in further studies, this microbicide could be a unique HIV prevention tool for women who are not able to negotiate other HIV prevention methods with their male partners. USAID continues to work with all partners to ensure that this new technology becomes available to vulnerable women and girls as soon as possible.

USAID also is continuing to evaluate the safety and effectiveness of pre-exposure prophylaxis (PrEP) for women, using oral Truvada – a combination of Tenofovir and emtricitabine – in what is known as the FemPrEP trial. This microbicide product is also antiretroviral (ARV)-based and is delivered orally, which potentially may increase both user compliance and product effectiveness. The FemPrEP trial is expected to enroll 3,900 women at sites in Kenya, Tanzania, and South Africa, and will be completed in 2012, as further discussed in Table 2.

Table 1. USAID Cooperative Agreements for Microbicide Research and Development

USAID Cooperating Agency	FY06 Funding ($ thousands)	FY07 Funding ($ thousands)	FY08 Funding ($ thousands)	FY09 Funding ($ thousands)	FY10 Funding ($ thousands)
Population Council	7,150	7,227	6,505	7,317	8,000
CONRAD	14,097	13,982	13,506	15,560	12,000
Family Health International	13,776	12,551	14,914	16,683	17,510
WHO	100	406	837	700	600
Global Campaign for Microbicides	735	728	905	919	800
Int'l Partnership for Microbicides	2,347	2,500	3,269	1,000	3,750
CDC	623	1,405	2,715	1,120	500
PATH	286	676	1,004	1,075	458
AIM Project	186	125	351	253	0
Alliance for Microbicide Development	300	0	580	323	0
GH Tech	0	0	50	50	30
CAMI	0	0	0	0	352
Biomed APS (Partners TBD)	0	0	0	0	1,000
TOTAL	**39,600**	**39,600**	**44,636**	**45,000**	**45,000**

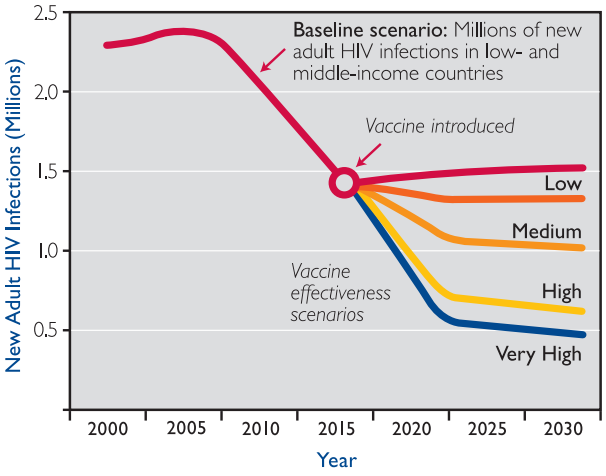
Table 2: Phase IIB/ III Microbicide Studies Currently Supported by USAID

	Tenofovir 1% Vaginal Gel	Oral Truvada in Women
Location of Sites	South Africa	Kenya Tanzania South Africa
Start of Screening and Enrollment	May 2007	July 2008
Number of Participants Enrolled	889	3,900
Final Report Expected	Mid FY 2010	Early FY 2012
USAID Partner Conducting Trial	Family Health International, CONRAD, CAPRISA	Family Health International

Other next-generation ARV-based microbicide leads are in the product development pipeline and will be tested clinically if they continue to show good results in preclinical testing. USAID's support for the International Partnership for Microbicides is particularly instrumental in advancing these early and promising leads.

In accordance with USAID's strategic plan, during the next year, a large part of the Agency's microbicide development R&D budget will continue to support clinical studies of promising products. The remaining funds will be used to advance research on selected next-generation microbicide leads; novel delivery methods (such as vaginal rings, tablets, and films); combination products that include both multiple mechanisms of action and multiple-purpose agents (to prevent pregnancy and STIs as well as HIV); understanding and prevention of the risk of viral resistance; novel non-ARV leads; and optimized clinical trial design and trial site coordination. Some funds also will be used to prepare for the policy and regulatory requirements that will need to be addressed for the approval and introduction of these new products when they are shown to be safe and effective.

Figure 1. Possible Scenarios for the Impact of an HIV Vaccine



Source: International AIDS Vaccine Initiative. (2009). Estimating the impact of an AIDS vaccine in developing countries. *IAVI Insights*, Policy Brief 20. Available from http://www.iavi.org/publications-resources/Pages/PublicationDetail.aspx?pubID=5ebd3b8f-532f-44fa-8bbc-d2d3e14fb2e6.

Vaccine Development

Adding an effective AIDS vaccine to a comprehensive prevention strategy holds the most hope for diminishing the HIV pandemic (Figure 1). Since 2001, USAID has funded the International AIDS Vaccine Initiative (IAVI), a nonprofit organization that acts as a virtual pharmaceutical company to accelerate the development and clinical testing of HIV vaccine candidates (Figure 2).

Under a five-year cooperative agreement initiated in 2006, USAID is supporting IAVI 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 issues. USAID-supported IAVI research has provided vital information on a variety of factors affecting the HIV vaccine field, such as regulatory and licensing issues, normative laboratory values in African populations, new strategies to engage biopharmaceutical companies in HIV vaccine development, and preparation for the manufacture and distribution of vaccines once they are proven effective.

The goal of all vaccines is to create an immunological response that can either prevent infection or minimize the symptoms and course of a disease. Most vaccines work by neutralizing the infectious agent with antibodies, then eliminating the agent and/or infected cells; however, because HIV evades immune responses, infection by the virus does not usually result in the body's creation of protective antibodies. Also challenging is HIV's high rate of genetic variability, which may render a vaccine effective against only some forms of the virus. Innovative approaches to understanding both viral behavior and the human immune response are necessary for developing a globally relevant HIV vaccine.

Translating findings from the unique immunological response of rare HIV-resistant individuals who are able to generate broadly neutralizing antibodies holds great promise for producing a viable vaccine. As was published in the September 2009 issue of *Science*, USAID-supported IAVI studies led to the discovery of the first two broadly neutralizing antibodies capable of blocking HIV – these protective proteins were isolated from an African donor. Of note is the subsequent discovery of another powerful antibody at the Vaccine Research Center of the National Institute of Allergy and Infectious Diseases (NIAID), which received global press in July 2010. IAVI is collaborating with key scientists to develop these promising results, ultimately to design vaccine candidates that can prompt the immune systems of vaccinated individuals to produce similar antibodies before they are exposed to HIV, thus protecting them from infection. Once these investigational vaccines are ready for human trials, they will be tested in the network of clinical research centers USAID supports in Africa through IAVI, some in col-

laboration with the National Institutes of Health and the U.S. Department of Defense.

Another method used to develop candidate HIV vaccines focuses particularly on a few essential areas of viral behavior to inform and accelerate vaccine discovery. A USAID-supported IAVI study provided the first evidence that a new vaccine technique using a replicating rhesus cytomegalovirus vector could effectively control viral replication, actually aborting infection in vaccinated animals. This novel candidate vaccine is attracting global attention due to its ability to reduce HIV in the blood to undetectable levels in more than half of the infected animals. These findings have prompted IAVI to establish a clinical development program for human cytomegalovirus vector vaccine candidates, supported by USAID.

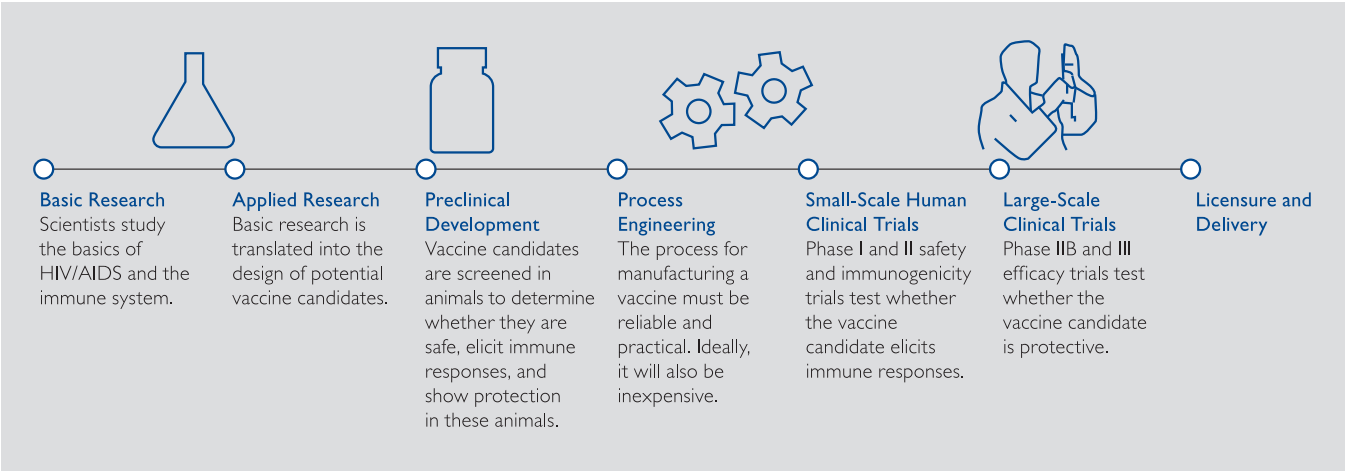
USAID supports studies to establish reliable HIV/AIDS incidence and prevalence estimates, enabling informed decisions on where large-scale efficacy trials may be possible. The Agency builds and strengthens local capacity at trial sites in human resources, laboratory, clinical, information technology, and other sustainable infrastructure capable of accelerating clinical trials of HIV/AIDS vaccines in developing countries. USAID advisors guide IAVI to establish referral patterns that interface with existing U.S. Government programs for HIV/AIDS treatment, care, and prevention services under the Global Health Initiative, the U.S. President's Emergency Plan for AIDS Relief, and the Global Fund to Fight AIDS, Tuberculosis and Malaria. Lastly, analytical models to forecast estimates of global demand for AIDS vaccines are being funded to prepare the field for eventual efficient product introduction and distribution.

Applied Research and Public Health Evaluation

USAID carries out HIV/AIDS program research and public health evaluations through established partnerships with universities and research organizations. These research programs aim to improve program coverage, quality, and effectiveness in developing countries as well as strengthen local capacity in HIV/AIDS operations research and public health assessments through training and in-country collaborations. Major tasks under these mechanisms include:

- Evaluation of service delivery models for HIV/AIDS prevention, care, and treatment programs
- Applied research to investigate effectiveness of interventions and translate results into public health guidelines
- Development of international standards and measures for the purpose of program monitoring and evaluation
- Systematic analyses of clinical, community-level, and population-based epidemiologic, demographic, and surveillance data
- Development and application of new technologies and intervention models for resource-poor settings

Figure 2. Process of HIV Vaccine Research and Development



Source: International AIDS Vaccine Initiative. (2008). From USAID, "Pathways of Discovery: HIV Vaccine Research and Development" (online). Available from http://www.usaid.gov/our_work/global_health/aids/TechAreas/research/vaccinefactsheet.html.

USAID is supporting research on orphans and vulnerable children (OVC) comprehensive action research, which aims to increase the evidence base for promising OVC program models. Orphans and vulnerable children may be at an increased risk for HIV infection, psychological distress, malnutrition, economic hardships, exploitation, trafficking, and other vulnerabilities. OVC-CARE studies will address these issues through rigorous, independent synthesis of experiences to date and evaluation research that investigates program processes, outcomes, and impact indicators.

USAID also is supporting a study that is developing and testing a multicomponent program model for reducing adolescent girls' vulnerability to HIV/AIDS. This initiative goes beyond typical HIV prevention interventions that focus on the individual to account for the interconnected role of social structural conditions in individual vulnerability.

Another USAID project dedicated to HIV prevention is Research to Prevention (R2P), which aims to improve HIV prevention programs in countries most affected by the HIV epidemic. R2P is undertaking applied research and program evaluation to identify interventions that successfully increase access to and quality of HIV prevention services, and address knowledge gaps in HIV prevention programming. R2P is dedicated to the utilization of research to guide programs and influence policy. As part of this project, studies are being conducted in a number of countries to optimize volume, integration, and efficiency of male circumcision service delivery. While male circumcision can be an important part of HIV prevention programs, it must be safely provided, integrated into, and not substituted for HIV/AIDS prevention programs. Another study under this project involves evaluating program models addressing concurrent sexual partnerships. In addition, the project is assessing prevention programs in developing countries to clarify what works and is developing methodologies to improve measurement of self-report data on sexual behaviors.

Key Partners in HIV/AIDS Research and Introduction

Alliance for Microbicide Development

Bill & Melinda Gates Foundation

Boston University

CAMI

Center for the AIDS Program of Research in South Africa (CAPRISA)

CONRAD

Crucell

Elizabeth Glaser Pediatric AIDS Foundation

Family Health International

Futures Group

GH Tech

Global Campaign for Microbicides

Global Fund to Fight AIDS, Tuberculosis and Malaria

Global HIV Vaccine Enterprise

ICF Macro

International AIDS Vaccine Initiative

International Clinical Epidemiology Network

International Partnership for Microbicides

Jhpiego

Johns Hopkins University

MasiMax Resources, Inc./RTI International/AIM Activity

National Institutes of Health: NIAID; Eunice Kennedy Shriver National Institute of Child Health and Human Development; Office of AIDS Research

PATH

Population Council

Population Services International

Synergy Project

University of North Carolina at Chapel Hill

University of the Witwatersrand (South Africa)

U.S. Centers for Disease Control and Prevention

U.S. Food and Drug Administration

U.S. Military HIV Research Program

U.S. President's Emergency Plan for AIDS Relief

World Health Organization

Malaria

Areas of Research and Introduction: Five-Year Strategy 2006–2010	FY 2010 Funding
Vaccines	$7,230,000
New Drugs, Formulations, and Approaches	$2,800,000

Issues and Rationale

Malaria remains one of the major public health problems in Africa. It is estimated there are between 300 million and 500 million cases and about 900,000 deaths from the disease each year, with 90 percent of those deaths in African children under 5 years of age. Malaria places a tremendous burden on national health systems and individual families. It is estimated that malaria accounts for approximately 40 percent of public health expenditures in Africa and causes an annual loss of $12 billion, or 1.3 percent of the continent's gross domestic product.

Approximately 3.2 billion people worldwide live in areas at risk of malaria transmission. Although anyone living in such areas can be infected, three populations are particularly vulnerable: children under 5, pregnant women, and people living with HIV/AIDS.

USAID, through the President's Malaria Initiative (PMI), is working to reduce malaria-related deaths by expanding coverage of four proven cost-effective malaria prevention and treatment intervention strategies:

1. Insecticide-treated nets

2. Indoor residual spraying

3. Diagnosis of malaria and provision of treatment with artemisinin-based combination therapy (ACT)

4. Intermittent preventive treatment for pregnant women

Initial PMI focus country data show a decrease in the incidence and prevalence of malaria in areas where these interventions have been applied and a significant reduction in under-5 child mortality rates (Figure 1). Despite this progress, increased resistance to both antimalarial drugs and insecticides has created a need for new technologies and tools that can improve and maintain malaria control efforts.

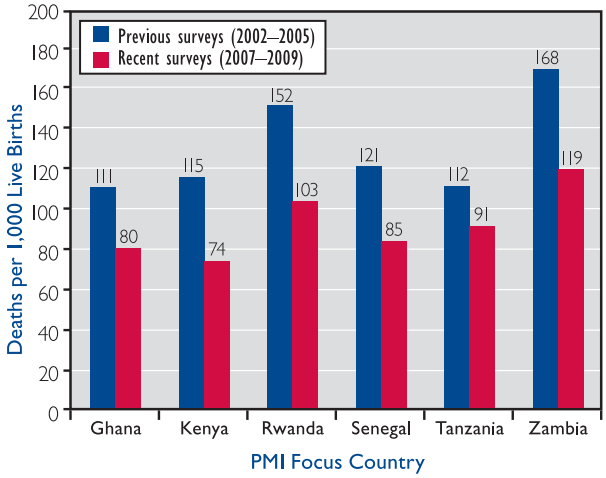
Areas of Research and Introduction

USAID supports malaria research through a coordinated and collaborative approach among intergovernmental U.S. agencies – such as the U.S. Centers for Disease Control and Prevention (CDC), Walter Reed Army Institute of Research (WRAIR), NIAID, and Naval Medical Research Center – as well as other research partners around the globe. USAID malaria control and prevention research focuses on:

- Vaccine development and evaluation

- Novel drug development to address resistance

Figure 1. Reductions in All-Cause Mortality Rates of Children Under 5 in Six PMI Countries



Source: U.S. Agency for International Development/PMI. (2010). *The President's Malaria Initiative: Sustaining Momentum Against Malaria: Saving Lives in Africa – Fourth Annual Report*, April 2010. Available from http://www.fightingmalaria.gov/about/index.html.

Vaccines

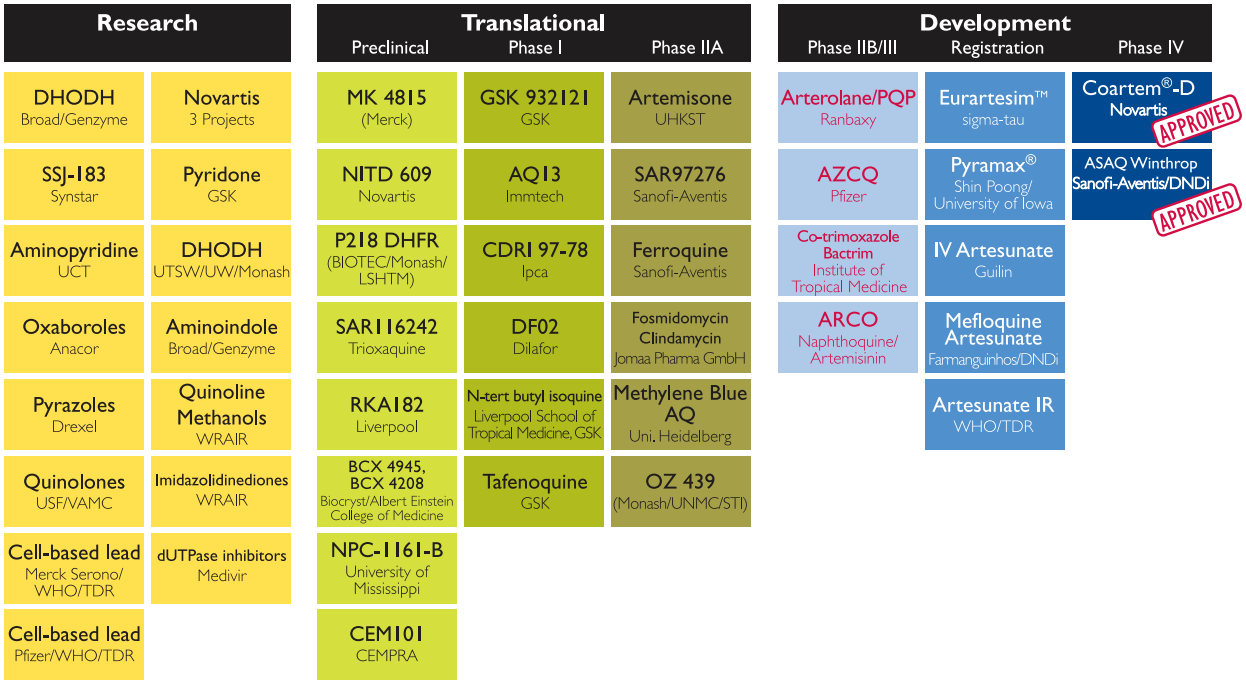
The USAID Malaria Vaccine Development Program (MVDP) aims to develop vaccines that will reduce malaria mortality and morbidity in residents of endemic countries, especially children under 5 and pregnant women. The MVDP focuses on vaccines that prove to be highly effective in very young children, have a long duration of efficacy, are suitable for deployment in the developing world, and are cost-effective.

Early USAID MVDP support contributed to the development of the most advanced malaria vaccine to date: the GlaxoSmithKline (GSK) Biologicals vaccine RTS,S/AS01b, which has been shown to be safe, has a 50 percent protective efficacy and can be safely co-administered with routine child immunizations. Phase III evaluation trials of this vaccine have begun in seven African countries. The vaccine is on track for licensure, perhaps as early as 2015. However, 50 percent protection leaves one-half of children vulnerable to malaria, and vaccines with greater efficacy are needed. The USAID MVDP remains focused on filling in existing research gaps by improving promising vaccines and developing alternative vaccines using different mechanisms and formulations.

In Mali, USAID MVDP supported the pediatric efficacy trial of the FMP2.1/AS02a malaria vaccine, in collaboration with WRAIR, GSK, NIAID, the University of Maryland's Center for Vaccine Development, and the University of Bamako Malaria Research and Training Center. This vaccine consists of the Apical Membrane Antigen 1, produced by WRAIR and formulated with the GSK adjuvant AS02a. Though the overall efficacy of the vaccine was low, a 70 percent efficacy was observed when only parasites similar to those on which the vaccine is based were analyzed, suggesting an increased protective effect of a complex Apical Membrane Antigen 1 vaccine that is based on multiple parasite types. Building on these results, USAID is supporting studies to determine the number of components required to enable the Apical Membrane Antigen 1 vaccine to protect most children from various parasite types. These investigations are scheduled to be completed in 2011, after which the feasibility of producing such a multivalent vaccine will be evaluated.

In Kenya, USAID MVDP supported an adult safety and immunogenicity trial of another vaccine produced by WRAIR and formulated with a GSK adjuvant, FMP010/AS01b. This vaccine, based on the major

Figure 2. MMV Global Malaria Portfolio



Source: Medicines for Malaria Venture. (2010). "Global Malaria Portfolio, 2nd Quarter, 2010." Available from http://www.mmv.org/research-development/project-portfolio.

merozoite surface antigen of the malaria parasite MSP1, was evaluated to determine if it was more immunogenic against multiple parasite types than the previously field-tested MSP1 vaccine FMP1/AS02a. The vaccine did not meet criteria for further development and will not be tested further as a stand-alone vaccine. The results underline the likely requirement for a multivalent approach for MSP1- as well as Apical Membrane Antigen 1-based vaccines.

USAID is supporting the U.S. Naval Medical Research Center's efficacy trial of a vaccine that stimulates cellular immunity by eliciting an attack on parasites by cells rather than by antibodies. This controlled trial involved the artificial infection of subjects with laboratory-bred mosquitoes that carried specific malaria parasites. Induction of cellular immunity required more complex prime-boost vaccination schemes, which consisted of three injections: two DNA prime vaccines followed several months later by a boost injection. Results showed that four of the 15 subjects were completely protected from malaria, highlighting the promise of cellular immunity; however, the proportion of subjects protected was too small to consider the use of the regimen as a control tool. Another trial currently is being initiated to determine which aspects of the immunization regimen were responsible for the observed protection; this study will test specifically whether initial DNA "priming" is required. Based on the results, additional studies to determine the requirements for protection will be implemented. Parallel to this effort, USAID is also supporting the development of another prime-boost regimen involving two different adenoviruses produced by Crucell, through an agreement with the PATH Malaria Vaccine Initiative; the results will further elucidate the requirements for the induction of cellular immunity against malaria.

Emerging information from these and other studies suggests that a period of preclinical and early clinical development is now appropriate. Consequently, the USAID MVDP does not plan additional field trials during the next year; the objective is to re-enter trials of this type when there is confidence that a vaccine that could achieve licensure is available.

New Drugs, Formulations, and Approaches

Through malaria drug development research, USAID aims to accelerate the viability of appropriate treatments in developing countries. USAID has a two-pronged malaria drug development strategy: (1) discovery and development of new antimalarial drugs and drug formulations, especially those that will be affordable to populations living in malaria-endemic areas and target pregnant women and children under 5; and (2) operational and field research that lays the groundwork for the safe and effective use of existing and new antimalarial drugs and drug combinations by national malaria control programs.

Key Partners in Malaria Research and Introduction

GenVec, Inc.
GlaxoSmithKline PLC
Johns Hopkins University
Kenya Medical Research Institute
London School of Hygiene and Tropical Medicine
Malaria Research and Training Center
Medicines for Malaria Venture
National Institute of Allergy and Infectious Diseases
Partner government ministries of health
PATH Malaria Vaccine Initiative
University of Bamako (Mali)
University of Maryland, Center for Vaccine Development
U.S. Naval Medical Research Center
Walter Reed Army Institute of Research
WHO Special Programme for Research and Training in Tropical Diseases
World Health Organization

Since 2004, USAID has provided $1.5 million per year to the Medicines for Malaria Venture (MMV), a nonprofit public-private partnership created to replenish then sustain the global pipeline of antimalarial drugs. MMV's goal is to register at least one new malaria treatment every five years, with an emphasis on drugs that are effective against drug-resistant strains of *Plasmodium falciparum*, have a retail cost of less than $1, and can be used safely by young children and pregnant women. Research and development activities with MMV are carried out at a broad variety of institutions, comprising more than 100 academic, pharmaceutical, nonprofit, and endemic-country partners in 38 countries, including the United States. MMV currently has a portfolio of 60 different pharmaceuticals at various stages of development, from drug discovery to Phase III human field-testing and registration (Figure 2).

Through USAID support, a dispersible pediatric formulation of lumefantrine-artemether (Coartem®) was registered with Swissmedic in December 2008. It has since been approved for use in 21 malaria-affected countries. In addition, dossiers for dihydroartemisinin-piperaquine and pyronaridine-artesunate, two new and novel ACTs, were submitted to the European Union Regulatory Authority in 2009 and 2010, respectively; the submissions are expected to be approved soon.

In partnership with the WHO Special Programme for Research and Training in Tropical Diseases, USAID is also supporting drug-related research in the following areas:

- Prevention of malaria in pregnancy: Studies are under way to demonstrate the relative safety of ACTs in the second and third trimesters of pregnancy.
- Studies are assessing the effectiveness of integrating community-based malaria case management with pneumonia and diarrhea (two other major killers of children under 5).
- Studies are assessing the use of rapid diagnostic tests in the case management of malaria at the community level.

Tuberculosis

Issues and Rationale

Tuberculosis (TB) is a major global health threat that kills approximately 1.8 million people each year; more than one-third of the world's population is thought to be infected with TB. While TB is found in almost every country in the world, it disproportionately affects poor countries and marginalized populations. Eighty percent of estimated cases occur in just 22 developing and/or transitioning countries. Despite advances in TB prevention and treatment, multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB threaten to undermine recent progress in controlling this disease.

Over the past two decades, the global HIV epidemic has caused tremendous increases in the burden of TB in regions of high HIV prevalence, especially in sub-Saharan Africa. Not only are HIV-positive individuals at a higher risk of becoming infected with TB, but among people with latent TB infection, HIV infection is the strongest known risk factor for progressing to active TB disease. An estimated 30 to 40 percent of HIV-related deaths are due to TB.

Areas of Research and Introduction

The translation of research and development into programmatic norms is of strategic importance to USAID. The Agency has been a leading supporter of research activities that aim to have a direct effect on country-level TB programs while mitigating the risks of drug resistance by (1) reducing diagnostic delay; (2) reducing the duration and improving efficacy of treatment (including care of persons infected with TB and HIV); (3) preventing disease; and (4) increasing access to Directly Observed Treatment, Short-course (DOTS). USAID brings its field presence to TB research within these targeted areas by informing the research community about field-based needs and priorities, enabling field-based trials of new technologies, preparing the field for the introduction of new technologies, addressing barriers to access services, and translating the results of research into policy and practice.

New Drugs/Improved Regimens

Research to investigate new anti-TB drugs is critical because more effective, better tolerated, shortened regimens can dramatically improve patient outcomes, reduce the toll of TB on patients and their families, decrease the strain on health systems, and slow the development of MDR-TB. Approximately 20 percent of USAID's research funding for TB is used to support the evaluation of promising new drugs. USAID's comparative advantage is to contribute to research at the stage where it has direct implications for the field (clinical trials at Phase IIB and beyond). USAID is providing ongoing support to the Global Alliance for TB Drug Development (a public-private partnership) to continue Phase IIB and Phase III clinical trials of three novel anti-TB compounds designed to shorten the duration of TB treatment. A fourth drug is being evaluated through the WHO's Special Programme for Research and Training in Tropical Diseases. USAID-led clinical trials also aim to revise, refine, and maximize the impact of current treatment standards and regimens.

USAID currently is supporting a study that will test the efficacy of a nine-month, standardized regimen that uses existing drugs for MDR-TB treatment; a nine-month treatment regimen is significantly shorter in duration than the current standard regimen of 18 to 24 months. This Standardized Treatment Regimen of Anti-TB Drugs for Patients with MDR-TB study will generate the evidence to inform new MDR-TB treatment recommendations from global technical agencies regarding the use of affordable drugs to treat TB. Technical assistance is under way to carry out this clinical trial in Kenya, South Africa, Vietnam, Indonesia, India, and Peru, and an evaluation protocol has been developed.

USAID is supporting the CDC to carry out the Preserving Effective TB Treatment Study, which compares the effectiveness of WHO's Green Light Committee (GLC)-approved MDR-TB treatment programs with non-GLC-approved programs in preventing resistance to second-line anti-TB drugs used in the treatment of MDR-TB. In FY 2009, the target enrollment of 1,802 patients in the Preserving Effective TB Treatment Study was completed, and baseline specimens and data were collected. By comparing acquired resistance to second-line anti-TB drugs among MDR-TB patients in GLC and non-GLC programs, the study aims to inform global policy and country decision makers on the future direction of these programs.

Tuberculosis Research Strategy 2006–2010

Total FY10 Funding: $10,300,000	
Strategy Themes	**Areas of Research and Introduction: Five-Year Strategic Plan**
New Drugs	Identify and introduce new, shorter treatment regimens, new second-line drugs for resistant disease, and drugs compatible with antiretrovirals for HIV; supporting trials of drugs at Phase IIB and beyond
Improved Regimens	Evaluate different formulations and combinations of drugs (existing and new) for effectiveness and impact on resistance
New Diagnostics	Increase the sensitivity and specificity of existing diagnostic technologies in individuals with and without HIV infection
	Evaluate new diagnostic technologies that more easily detect TB in individuals with and without HIV infection, enable rapid detection of drug resistance, and detect latent TB infection; supporting trials of diagnostics at Phase IIB and beyond
New Vaccines*	Test a vaccine that prevents infection with TB; supporting trials of vaccines at Phase III and beyond
	Develop an effective vaccine to protect TB-infected individuals from developing TB disease; supporting trials of vaccines at Phase III and beyond
Improve the Care of Persons Infected with TB and HIV**	Improve diagnosis of TB among HIV-infected individuals
	Improve detection of latent TB in HIV-infected individuals
	Evaluate efficacy and safety of TB drug regimens used in combination with antiretrovirals, for children and adults
	Test approaches to increase HIV testing among TB patients as an entry point to care
	Determine effective initiation, duration, and programmatic impact of preventive-therapy regimens, in consideration of antiretrovirals use
Improve the Performance of and Accessibility to DOTS Programs	Monitor patterns of drug resistance, TB-HIV, and TB prevalence***
	Enhance laboratory and program readiness for the adoption of new tools
	Evaluate innovations in service delivery to improve case finding, increase access to treatment, and improve program performance
	Build and utilize capacity for clinical trials in priority countries
	Identify and address epidemiological risk factors for TB, such as tobacco and diabetes

* It is not anticipated that this work will begin until 2011.

** This work is supported under PEPFAR and is not included in the total research budget.

*** As much of this work is considered routine surveillance, costs are not included in the total research budget.

New Diagnostics

USAID research targets the development of innovative diagnostic tools and approaches that accelerate TB case detection, provide enhanced diagnostic sensitivity and specificity, and are feasible for use in low-resource settings, in addition to supporting the improvement of currently existing diagnostic methods.

As a result of USAID-supported research, light-emitting diode fluorescence microscopy and front-loaded diagnosis have been adopted into global policy by WHO and endorsed for use in country programs. Light-emitting diode fluorescence microscopy increases ease of use while simplifying maintenance compared to traditional fluorescent microscopy. "Front-loading" or "same-day diagnosis" allows for the collection and examination of consecutive sputum specimens as well as the provision of test results in one day, compared with the current practice of two to three sputum examinations taken over two days or more. These new tools may reduce laboratory workloads and turnaround time for test results as well, facilitating earlier initiation of treatment. USAID currently is supporting evaluations on the implementation and scale-up of light-emitting diode fluorescence microscopy in countries with a high burden of TB. A recent evaluation of light-emitting diode fluorescence microscopy in Tanzania resulted in the introduction of this tool in high-volume laboratories throughout the country.

Line Probe Assays recently have been recommended by WHO for the detection of drug-resistant TB in sputum smear-positive samples. USAID currently is supporting operational research around the implementation of Line Probe Assays in epidemiologically different field settings (South Africa, Brazil, and India). This study will use an impact assessment framework that was developed to simplify the evaluation of health system requirements for effective implementation of Line Probe Assays to define, group, and link the outcomes that will be addressed in the research. The study aims to produce useful information for national TB programs in countries that are undertaking or are planning to undertake rollout of Line Probe Assays technology and is expected to be completed by July 2012.

Along with its partners, USAID is using novel approaches to diagnostic modeling, which blend transmission modeling with health system modeling concepts to accelerate the introduction of TB diagnostic tools. By assessing the impact of new tools on transmission dynamics within different epidemiological settings in conjunction with health system impacts and requirements, this comprehensive modeling approach will provide targeted guidance for national-level decision makers in high-TB-burden countries regarding the packages of diagnostic tools most suitable for their specific needs and budgets. A prototype model that focuses on diagnostics for drug-sensitive TB has been designed using this new approach and will be submitted for publication by the end of 2010.

Key Partners in Tuberculosis Research and Introduction

Foundation for Innovative New Diagnostics

Global Alliance for TB Drug Development

International Union Against Tuberculosis and Lung Disease

Partner government ministries of health

Stop TB Partnership Working Groups

U.S. Centers for Disease Control and Prevention

WHO Special Programme for Research and Training in Tropical Diseases

Improved Performance of and Accessibility to DOTS Programs

Country-level operational research is central to the improved performance of TB programs. USAID supports operations research to assess country-specific barriers to implementation, develop innovative approaches, and guide the adoption and use of new tools in the context of a national TB program.

In India, USAID-supported studies that resulted in significant changes to the national TB control policy – a change from the definition of a TB suspect from having a cough for a period of three weeks to having a cough for a period of two weeks, as well as a reduction in the number of sputum specimens required for diagnosis of TB from three to two. The study findings demonstrated an increase in the identification of persons with symptoms of TB. Launched nationwide in 2009, the new policy will not only help to detect TB cases sooner, but it will also reduce the laboratory workload and make diagnostic testing more convenient for patients.

Improve the Care of Persons Infected with TB and HIV

USAID-supported research is addressing challenges to coordinated TB-HIV care and poor treatment compliance. An evaluation of adherence rates among patients with TB/MDR-TB and HIV/AIDS who are on concurrent or overlapping treatments is currently under way in South

Africa. A separate review is examining epidemiological trends, risk factors, and treatments related to poor outcomes among children and adolescents with drug-resistant TB. The study results will be used to develop more effective programs for pediatric and adolescent TB patients, especially those with HIV infection.

New Vaccines

USAID is committed to providing support to promising vaccines that have the potential to have the greatest impact on TB control. USAID will work closely with the National Institutes of Health and the vaccine community to support field trials of vaccines that have progressed to late phases of development research. Clinical vaccine candidates for TB have emerged only recently, and it is expected that this support may occur as soon as 2011.

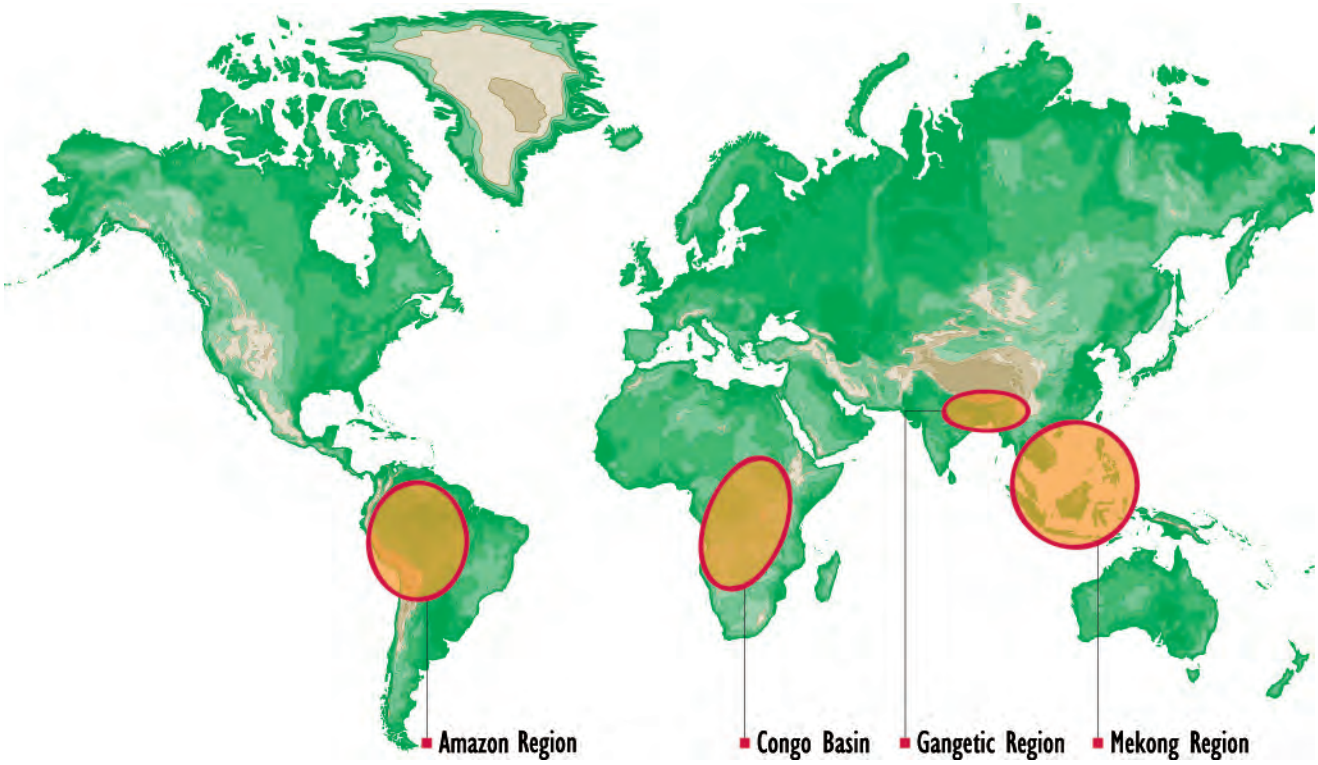
Emerging Public Health Threats

Nearly 75 percent of all new, emerging, or re-emerging diseases affecting humans at the beginning of the 21st century have originated in animals. Notable examples of such diseases, known as zoonotic diseases, include HIV/AIDS, severe acute respiratory syndrome, the pandemic H1N1 influenza virus, and H5N1 avian influenza (AI). The speed with which these diseases can emerge and spread presents serious threats to public health, economic growth, and development. The U.S. Agency for International Development (USAID) launched its Emerging Pandemic Threats (EPT) program in 2009 to mitigate these threats by identifying and responding to emerging zoonotic diseases at their source. The EPT program builds on USAID's leadership of international efforts to combat AI and bolster pandemic preparedness, as well as its critical support in response to the 2009 H1N1 influenza pandemic.

Predicting where new disease threats may emerge and detecting viruses and other dangerous pathogens before they spread to humans are critical to pandemic prevention. The EPT program targets geographic areas, known as "hot spots," where new disease threats have emerged in the past. These include the Congo Basin of East and Central Africa, the Mekong Region and other areas of Southeast Asia, the Amazon Region of South America, and the Gangetic Region of South Asia (see Figure 1).

Under the EPT program, USAID's PREDICT project is increasing local capacity in the geographic hot spots (Figure 1) to identify the emergence of new zoonotic diseases in high-risk wildlife such as bats, rodents, and nonhuman primates as well as conducting analysis to identify high-risk areas within the hot spot regions. In addition, PREDICT, in concert with WHO and the

Figure 1. USAID Emerging Pandemic Threats: Geographic Hot Spots



CDC, is developing protocols for a more active surveillance model. One of the major challenges facing early detection of new emerging diseases is compensating for the limitations of the current "syndromic surveillance" model. Considering diseases such as HIV/AIDS, where the time lapse between infection and onset of clinical symptoms can be decades, waiting for the onset of clinical symptoms to serve as the basis for picking up new emerging diseases could prove to be unsound.

Mindful of this challenge, one line of work in the EPT program will be to invest in a "predictive surveillance" model. This would consider environmental factors, potential points of disease transmission from animals to humans, and advances in genomics and informatics to classify new organisms on the basis of their risk of causing new diseases. This "predictive surveillance" model is intended to complement "syndromic surveillance" to build a significantly more comprehensive surveillance capacity for emerging disease threats.

Health Systems Strengthening

Issues and Rationale

Health systems strengthening research supports the development of effective, efficient, and equitable health systems through initiatives and strategies that lead to health improvement in the areas of access, coverage, quality, and efficiency. Consistent with the WHO, USAID views a health system as consisting of all organizations, people, and actions whose primary intent is to promote, restore, or maintain health. USAID advances research in the six core functions, or building blocks, of a working health system: service delivery; human resources; information; medical supplies, vaccines, and technology; health financing; and governance and leadership. In identifying the need for health systems improvements, USAID's approach is to look for constraints in quality, accessibility, or affordability and develop interventions within the framework of the six building blocks to address key gaps and bottlenecks. The challenges to high-quality, accessible, and affordable health services – and USAID's response through research – are summarized below.

Health Systems Strengthening Research Strategy 2006–2010

Total FY10: $15,424,383	
Strategy Themes	**Areas of Research and Introduction: Five-Year Strategy**
Service Delivery (Approaches and Technologies)	Make quality improvement an integral part of health care by documenting and raising its cost-effectiveness
	Spread improved health care practices through the health system
	Develop a knowledge management approach to encourage global sharing of improved practices
Health Workforce	Refine the methodologies used to assess the size and performance of human resources for health
	Identify the determinants of workforce productivity to inform global guidance and improve host country health workforce management
Information	Advance the area of monitoring and evaluation
	Engage with U.S. Government and international partners to provide highest quality data to inform health planning
Pharmaceuticals Management	Improve knowledge of the presence of substandard and counterfeit products on the market
	Explore their role in the emergence of drug resistance
	Improve logistics
Financing	Reduce gaps in access to essential services for most vulnerable populations
	Benchmark health systems performance through application of health systems assessment approach
Governance	Determine the best approaches for reducing corruption and increasing accountability within health sector
	Demonstrate that improved governance can contribute to increased utilization of priority health services

- In developing country service delivery models, critical functions of the health system often are challenged by inefficient standards and lack of evidence-based practices. Quality-improvement measures have been proven to be highly effective in the poorest health systems, but they often are not applied appropriately. Because these problems cannot be addressed by training alone, USAID's research has emphasized the development of quality-improvement collaboratives that enable peer-to-peer sharing of best practices in service delivery.

- Although the health workforce represents about 70 percent of the cost of health care, effective human resource development and management continue to be weak. Though well established, the general principles for maximizing workforce productivity need to be adapted to individual health systems. Producing more health workers is a key priority in many countries, but it must be part of a larger strategy that addresses recruitment and retention, increased efficiency, quality training, and effective human resource management systems. USAID is developing global guidance on the management of human resources for health, in collaboration with WHO and other United Nations partners, as well as pecuniary and non-pecuniary incentives to enhance worker productivity.

- Few developing countries have sufficiently effective health information systems, a key component to monitoring and evaluating health interventions as well as maximizing efficiency. Information systems are a critical tool for measuring progress toward health goals, identifying greatest gaps and needs, and enabling the efficient use of resources. An effective information system can support the evidence base for policy and strategy development and optimize allocation of scarce resources. USAID is improving data systems and quality and evaluating the effectiveness of information system investments and their impact on the health system.

- An estimated 30 percent of the world's population lacks regular access to medicines and other essential health supplies; this proportion rises to more than 50 percent in the poorest areas of Africa and Asia. Health systems with inadequate regulatory capacity are ill-equipped to control the entry of counterfeit and substandard medicines and products into the marketplace. Along with the inappropriate use of medicines, access to poor-quality medicines can contribute to the emergence of drug resistance and an increased need for second-line medicines, which can add to the cost and potential duration of treatment. USAID is raising awareness on the impact of substandard medicines on the quality of health care in developing countries and is developing tools to evaluate the effectiveness of quality assurance systems.

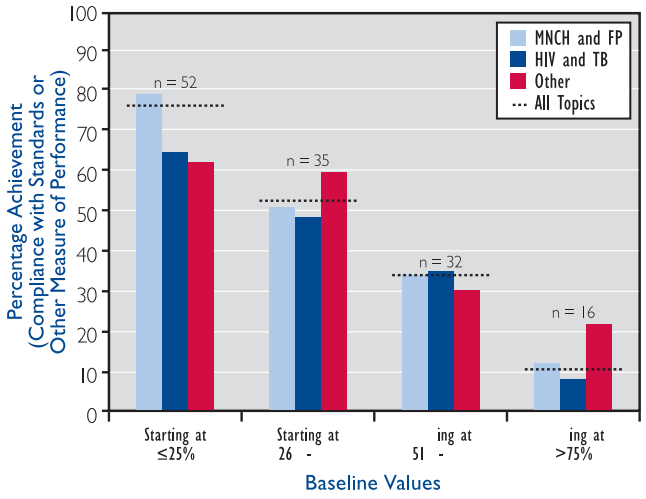
- Global estimates indicate that more than 180 million people in developing countries suffer from financial catastrophe due to high out-of-pocket health care expenditures and limited subsidies. Additionally, institutional and human capacity gaps in health finance systems result in inefficient resource allocation and weak financial oversight, leading to poorly managed and underfunded health systems. USAID supports increased access to costing information, efficient resource management allocation, sustainable financing strategies, sound financial policies, and effective oversight.

- Best practices in health governance involve financial stewardship, evidence-based policymaking, civil society participation, and effective leadership. The lack of participatory, transparent, and accountable governance hinders policy regulation and limits the effectiveness of health system performance; limited resources can exacerbate the problems of poor governance and corruption. According to Transparency International, 40 percent of the poorest countries in the world are also the most corrupt. USAID is developing methods for improved governance and leadership in resource-poor settings, including increased community-level oversight of health systems and strengthening of facility-level governance mechanisms.

Areas of Research and Introduction

USAID conducts health systems research and evaluations to identify and test improved practices and to facilitate host country introduction and scale-up of effective health interventions, which will reduce the burden of disease that most contributes to mortality and severe morbidity. USAID's health systems research meets four criteria: (1) It is relevant to the successful implementation of health interventions in HIV/AIDS, malaria, tuberculosis (TB), reproductive health and family planning (RH/FP), nutrition, and maternal, newborn, and child health (MNCH); (2) it has the potential to improve access, quality, and/or affordability; (3) it can achieve demonstrable and measurable results within three to five years; and (4) it is suitable for sustained use in low-resource settings.

Figure 1. Improvement Collaborative Performance-Level Achievements in 135 Measures of Compliance



Source: Franco, L.M., et al. (2009). Results of collaborative improvement: Effects on health outcomes and compliance with evidence-based standards in 27 applications in 12 countries. *Collaborative Evaluation Series*. Published by the USAID Health Care Improvement Project. Bethesda, MD: University Research Co., LLC.

Using Improvement Collaboratives to Strengthen Service Delivery

Modern quality-improvement approaches – long deployed in U.S. and European health care settings – offer methods for overcoming common barriers to quality care and delivering evidence-based standards. They have been proven to be effective in weak health systems that face severe financial, material, and human resource constraints. Using this approach, teams review and test changes in service delivery methods and evaluate the impact of these changes on the health system. Results from this process are shared among the teams and are used to inform global best practices in health service quality improvement (QI).

The degree to which providers follow national standards is a central measure of quality of care: Higher levels of compliance are strongly associated with better outcomes. A retrospective analysis of 27 quality improvement collaboratives in 12 countries reviewed the work of 1,338 teams on 135 measures of compliance with evidence-based standards and outcomes for MNCH, HIV/AIDS, TB, FP, and other areas. In baseline measures, these facilities provided care that, on average, met less than 50 percent of the national standards. After introducing approved changes, teams achieved performance levels of 80 percent or higher in 87 percent of the 135 measures of compliance. The teams with the lowest levels of initial quality were associated with the largest improvements (Figure 1). In addition, performance levels were sustained above 80 percent for an average of 13 months, indicating that teams participating in a collaborative approach can rapidly achieve significant sustainable improvements in quality of care and the important role this approach can play in strengthening health system performance.

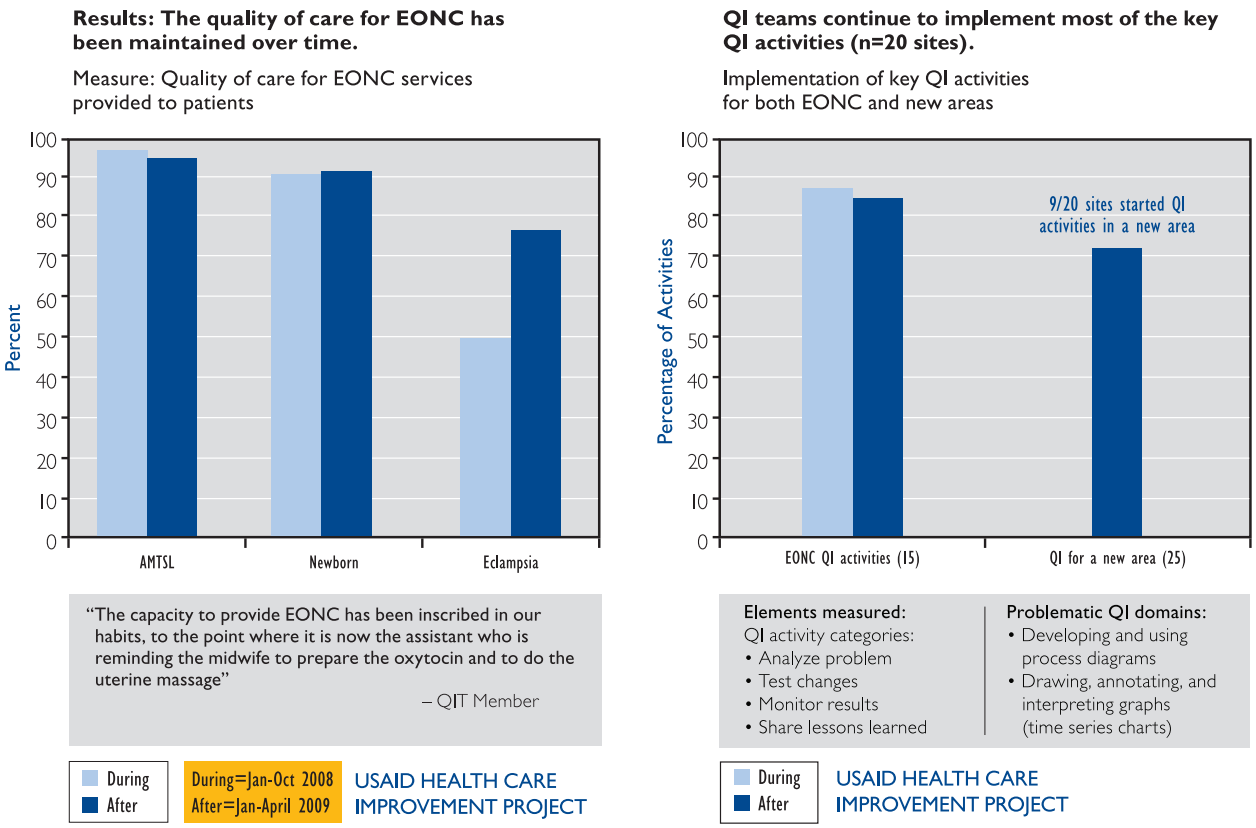
The institutionalization and spread of improvement practices and organizational models are needed to achieve sustainable results. Beginning in 2003, USAID has supported efforts to improve maternal and newborn services in Ecuador using the collaborative approach. An evaluation of a strategy to expand the implementation of best practices and QI to all facilities in the country is examining how well new facility-based teams, supported by provincial spread teams, are able to monitor indicators of quality and implement process changes to ensure compliance with standards in order to achieve effective essential obstetric and newborn care (EONC) services.

In Niger, where USAID has supported improved practices in EONC since 2006, a study on institutionalization found that participating facilities are maintaining gains in quality of care and, to some degree, implementation of basic QI activities (Figure 2), but staff mobility and a lack of active engagement hinder these achievements. Based on these results, the Ministry of Health (MOH) is implementing an institutionalization change strategy, which will be evaluated to assess sustainable gains in quality of care. Two similar studies have been initiated in Honduras and Nicaragua.

USAID is supporting studies in Nicaragua, Tanzania, Côte d'Ivoire, and Guatemala examining the role of peer-to-peer learning on exposure to, and uptake of, effective changes conducted by other improvement teams. The results of this work, expected in late 2010, will be used to strengthen the effectiveness of peer-to-peer learning as central to the collaborative approach.

To date, more than 1,300 improvement teams have been established in 12 countries, with a resulting impressive effect on service quality. Continuing research will identify how best to roll out the practice of improvement collaboratives within and between countries and overcome exogenous barriers to sustainable QI.

Figure 2. Institutionalization of EONC-Improved Practices in Niger



Source: USAID Health Care Improvement Project.: University Research Co., LLC

Improving Health Workforce Capacity and Productivity

USAID's health workforce research aims to identify innovative approaches to maximize the effective use of human resources and increase the efficiency and capacity of the health workforce. Resource-limited countries have been exploring ways to redeploy their health workforce, with an emphasis on identifying evidence-based approaches to rationalize the mix of personnel types and skill sets. This often involves task shifting from physicians and nurses, known as skilled health care workers, to unskilled providers such as clinical officers either to gain efficiencies in care delivery or to expand coverage of high-impact interventions. In Benin, a non-inferiority study on the reallocation of maternal and newborn counseling evaluated the quality and impact of counseling by skilled and unskilled health care workers in 14 Government facilities, following the introduction of job aids and task shifting. Job aids were found to be acceptable and consistent with existing practices, and delegation of tasks to less skilled cadres was shown to improve provision of care. This work will help to inform policies regarding the allocation of tasks related to maternal and newborn counseling in Benin and other countries with similar contexts.

USAID is developing a productivity improvement model, including a package of measures and tools, to improve outputs at what are traditionally less productive times for facility use. This builds upon workforce-productivity studies conducted by the Agency in Zanzibar and by the Tanzanian National Institute for Medical Research to determine productivity levels and correlates of increased productivity as a basis for global guidance. In Zambia, a study is assessing changes in productivity, the ease of use, and the sustainability of productivity improvement processes in six facilities. Each facility designed an improvement process based on its identified needs and causes of productivity gaps. Selected interventions included clear codes of conduct, the development of job descriptions, resource pooling, and skill-building

activities. Positive results from this study will demonstrate the effectiveness of a sustainable approach to increasing the productivity levels of existing health care workers.

While financial incentives for performance are thought to be effective, questions remain regarding their sustainability. USAID is supporting an assessment of the impact of nonmonetary incentives on HIV counseling and testing performance and provider retention in Swaziland. A separate study in Ethiopia is evaluating the impact, feasibility, and effectiveness of providing financial versus nonfinancial incentives on performance, contingent on providers meeting predefined HIV counseling and testing targets. Findings from these studies will inform on strategies to address health worker performance and retention issues effectively, as well as demonstrate the comparative effectiveness and side effects of monetary versus recognition systems, respectively.

It regularly is taken for granted that providers at faith-based facilities perform better, often for less pay, because of the intrinsic motivation of providing care as a mission. A study is comparing motivation and performance factors affecting the same cadre of health workers in the faith-based and public sector facilities in Uganda and Malawi. A preliminary analysis suggests that performance, retention, and intrinsic motivation at faith-based organization facilities may not be much higher than at public facilities.

USAID is developing a new tool to evaluate the functional performance of community health workers (CHWs); ongoing field tests in Nepal, Benin, and Zambia are being conducted to validate the tool. Once finalized, it will be used to monitor and strengthen community-based maternal and child health (MCH), HIV/AIDS, and malaria programs worldwide. This will be an important step for formalizing CHWs into the health systems and for ensuring that CHWs are delivering interventions routinely, effectively, and with high quality.

A rapid assessment tool is being developed and tested to address implementation barriers related to human resource management. Building upon the Health Workforce Action Framework, this new tool includes an approach to country-based human resources for health leadership group strengthening, policy implementation, and monitoring.

Introducing New Methods for Information Management

The Monitoring and Evaluation Systems Strengthening Tool, developed collaboratively by USAID and other global leaders in information systems, continues to be used widely by the Global Fund to Fight AIDS, Tuberculosis and Malaria, especially for assessments of malaria and TB systems. For HIV/AIDS, the Monitoring and Evaluation Systems Strengthening Tool largely has been superseded by the 12-component monitoring and evaluation (M&E) system assessment tool developed collaboratively by USAID, the Joint United Nations Program on HIV/AIDS (UNAIDS), the World Bank, and other groups. The 12 components of the M&E assessment tool build on the Monitoring and Evaluation Systems Strengthening Tool as well as other assessment tools and represent a harmonized M&E system assessment tool for HIV/AIDS. Ongoing work is documenting the use of this tool in Nigeria toward forming a global community of practice.

Despite widespread consensus on the importance of routine health information systems (RHIS) as a contributing factor in improving health systems performance, there has been little research on the effectiveness of investments made to strengthen RHIS, on the quality and use of the data produced, and their influence on health systems performance. USAID is supporting an evaluation of the impact of RHIS-strengthening interventions on RHIS and health systems performance at the regional, district, facility, and community levels.

As part of the Agency's continuing priority to provide the highest quality data to inform global HIV/AIDS efforts, USAID's Demographic and Health Surveys and AIDS Indicator Surveys are important sources for global efforts coordinated by UNAIDS to estimate HIV/AIDS prevalence among the general population. USAID partners also have created statistical models to estimate the HIV prevalence rates of nonhousehold populations such as inmates, the homeless, and sex workers.

Understanding and Protecting the Effectiveness of Medical Products

The sale of counterfeit, altered, and poor-quality malaria drugs is particularly acute in developing countries due to the limited regulatory capacity of country health systems and their inability to control the entry of antimalarials into the marketplace. USAID supported a collaborative WHO-U.S. Pharmacopeia Drug Quality and Information Program study that documented quality control failure rates of antimalarials sampled from public, private program, and informal providers in Senegal (44 percent), Madagascar (30 percent), and Uganda (26 percent). More than 500 academic and professional media outlets worldwide have reported on the study results, which are being used in policy advocacy to strengthen quality assurance systems and regulatory frameworks.

USAID also is supporting the development of a tool to enable national regulatory authorities to evaluate their quality assurance systems and to prioritize corrective actions to purchase medicines of good quality.

Improving Evidence and Practice in Health Financing

USAID's investment in research on health financing focuses on increasing evidence of successful approaches to financially sustainable and equitably distributed health care services in developing countries. Research on user fees, national health accounts (NHA), and program sustainability analyses have and will continue to inform health finance strategies in resource-poor settings.

User fee elimination policies can ensure that systemic barriers to accessing services are alleviated for the poorest individuals. USAID-supported research in Mali is assessing the impact of subsidies on cesarean deliveries; preliminary results indicate that health facility staff support the provision of free cesareans and that staff shortages and supply stockouts have not posed a major problem. However, limited and incorrect knowledge about the subsidies, difficulty traveling to first-level facilities, and perceptions of low-quality care contribute to limited use of and access to institutional deliveries and cesareans.

Building on the existing evidence, a study in Senegal and Mali is assessing the program and policy implications of applying user fees for malaria services and the rationale, impact, and challenges in implementing a user fee waiver for malaria services for children under 5. This research will inform programs on whether user fees should be removed or sustained for malaria treatment, especially for children under 5 years of age, in these two countries.

The NHA methodology was developed by USAID in collaboration with global partners, including the World Bank, the Organisation for Economic Co-operation and Development, WHO, and the Swedish International Development Cooperation Agency, to measure total – public, private, and donor – national health expenditures. In 2010, USAID has continued to support the use of this tool to measure spending in national accounts and subaccounts and is working with more than 25 countries to standardize and institutionalize NHA through sustained production and use of NHA data. In Armenia, NHA data convinced policymakers to triple the country's FY 2009 budget allocation for RH and antenatal care, and NHA data encouraged Georgia to increase its health insurance coverage for the poor. To better support such efforts, an NGO/donor database is being developed

Key Partners in Health Systems Strengthening Research and Introduction

Abt Associates

Academy for Educational Development

Alliance for Health Policy and Systems Research

Alliance Group (Malawi)

Bill & Melinda Gates Foundation

Danida

Global Alliance for Vaccines and Immunizations

Global Drug Facility

Global Fund to Fight AIDS, Tuberculosis and Malaria

Global Health Workforce Alliance

Green Light Committee

Health Metrics Network

Health Research Department of Ghana Health Service

ICF Macro

IntraHealth International

Irish Aid

Management Sciences for Health

Ministry of Health/TRAC Plus, Malaria Unit (Rwanda)

Miz-Hasab Research Center (Ethiopia)

Open Society Institute

Organisation for Economic Co-operation and Development

Partner government ministries of health

Stop TB Partnership Working Groups

Swedish International Development Cooperation Agency

The Partnership for Child Health Care, Inc./BASICS

U.K. Department for International Development

UNAIDS

UNFPA

University Research Co., LLC

U.S. Centers for Disease Control and Prevention

U.S. Pharmacopeia Drug Quality and Information Program

U.S. President's Emergency Plan for AIDS Relief

World Bank

to provide vital financial information that can be used for planning and M&E. Currently being piloted in Rwanda, this unique approach builds local capacity and ensures local MOH staff will be able to continue data collection and use in the future.

Computer-based analytic tools, developed with USAID support, have improved the availability and quality of data for policymakers in the health sector. The HIV/AIDS Program Sustainability Analysis Tool and the SPECTRUM suite of models have been supporting resource allocation decisions by partner governments involved in planning a national response to HIV/AIDS. USAID continues to support the increased use of these models in Africa, Asia, and Latin America.

Performance-based incentives are being implemented in a number of developing countries to encourage the use of priority services and to stimulate quality. However, concerns remain that introducing incentives to promote FP could interfere with a client's voluntary choice. At the same time, when incentives are linked to the use of other services, there is a danger that FP may be neglected. USAID has supported research to evaluate the importance and potential benefits of performance-based incentives schemes in FP. The results of the work included guidance for USAID Missions, partners, and country implementers on responsible programming of incentives linked to quality FP services.

Assessing and Improving Health Governance

USAID is advancing research to better understand country needs on and successful approaches to health system governance and leadership. Previously, USAID supported a comparative analysis of data from the System-Wide Effects of the Global Fund assessments conducted in Benin, Ethiopia, and Malawi, which indicated that with the rapid launch of new services, more remains to be understood about the impact of the Global Fund on the countries' health systems. Studies conducted by the Global HIV/AIDS Initiatives Network builds on the outcomes of this work.

USAID supported the development and testing of Quality Assurance Partnership Committees (QAPCs) in the Philippines. QAPCs are an innovative approach toward improving MCH services by strengthening facility-level governance mechanisms. These committees bring together local leaders and government officials, health care providers, civil society, and community representatives to address issues and challenges related to access, availability, and the quality of services at facilities. QAPCs provide a forum for communities to voice concerns while holding local officials and providers accountable for the services delivered. The results of this research will inform on the feasibility of QAPCs within the Filipino context as well as document their effect on access, utilization, and the quality of MCH services.

USAID is continuing its collaboration with international agencies to improve the evidence base for benchmarking health system performance. A health systems database that consolidates key demographic, health status, economic, and governance indicators was launched in 2008. This easy-to-use Web-based tool compiles and analyzes country and regional data from multiple sources and provides policymakers with an overview of a country's health system performance. In the FY 2010 release, substantial information is being added for several major health issues, including HIV/AIDS, TB, malaria, MCH, and RH. One-page dashboards displaying health and key system indicators will enable users to view data from a broad system perspective. The health systems database is used in conjunction with the health systems assessment approach, which examines multiple health system components, compiles and synthesizes data, and provides a guide for leaders and policymakers to target key priorities in health systems strengthening.

Addendum 1: Core Funding for Targeted Health Issue Strategies[1]

Health Issue	Product	FY 2006 Obligated Funds	FY 2007 Obligated Funds	FY 2008 Obligated Funds	FY 2009 Obligated Funds	FY 2010 Funding
HIV/AIDS	Vaccines	$28,710,000	$28,710,000	$28,477,000	$28,477,000	$28,710,000
	Microbicides	$39,600,000	$39,600,000	$44,635,500	$45,000,000	$45,000,000
	Global Leadership in HIV/AIDS Applied Research and Public Health Evaluation	$1,750,000	$3,250,000	$3,900,000	$3,900,000	$4,625,000
	Total	**$70,060,000**	**$71,560,000**	**$77,012,500**	**$77,377,000**	**$78,335,000**
Malaria	Vaccines	$6,200,000	$7,000,000	$7,000,000	$6,950,000	$7,230,000
	New Drugs, Formulations, and Approaches	$3,200,000	$3,000,000	$3,000,000	$2,100,000	$2,800,000
	Total	**$9,400,000**	**$10,000,000**	**$10,000,000**	**$9,050,000**	**$10,030,000**
Tuberculosis	New Drugs	$2,400,000	$3,000,000	$3,000,000	$3,000,000	$3,000,000
	Improving Performance of and Access to DOTS,[2] Including Diagnostics	$2,790,000	$4,662,090	$4,500,000	$6,400,000	$7,300,000
	Total	**$5,190,000**	**$7,662,090**	**$7,500,000**	**$9,400,000**	**$10,300,000**
Emerging Pandemic Threats[6]	**Total**	–	–	–	–	**$5,000,000**
Family Planning and Reproductive Health	Contraceptive Technologies	$10,500,000	$13,630,000	$10,223,000	$13,071,000	$9,965,000
	Improved Use and Services Delivery	$14,000,000	$15,660,000	$19,450,000	$17,126,000	$13,370,000
	Total	**$24,500,000**	**$29,290,000**	**$29,673,000**	**$30,197,000**	**$23,335,000**
Maternal and Newborn Health	Healthy Pregnancy and Birth Care Outcomes	$1,283,000	$1,634,000	$1,634,000	$865,000	$1,019,080
	Maternal Mortality and Morbidity Measurement Tools	$130,000	$122,000	$122,000	$0	$0
	New Pregnancy and Birth Interventions and Introduction	$4,065,000	$2,700,000	$2,700,000	$4,000,236	$4,255,000
	Neonatal Research and Newborn Care Practices	$1,600,000	$2,552,000	$2,552,000	$3,749,150	$3,835,000
	Total	**$7,078,000**	**$7,008,000**	**$7,008,000**	**$8,614,386**	**$9,109,080**
Nutrition	Vitamin A Deficiency Prevention and Control[3]	$759,000	$350,000	$350,000	$400,000	$500,000
	Iron-Anemia Prevention/Rx Packages	$376,600	$380,810	$380,810	$580,810	$750,000
	CMAM (formerly Community Therapeutic Care)	$1,100,000	$1,200,000	$1,200,000	$1,000,000	$1,200,000
	Dietary Quality and Diversity	$0	$150,000	$600,000	$700,000	$1,650,000
	Antenatal Multiple Micronutrient Supplementation	$180,000	$0	$0	$0	$0
	Total	**$2,415,600**	**$2,080,810**	**$2,530,810**	**$2,680,810**	**$4,100,000**
Child, Environmental, and Urban Health	Community-Based Pneumonia Treatment	$650,000	$638,000	$638,000	$1,264,350	$1,318,000
	Diarrhea Management: Reversing Declining Rates of Use of ORT[4]	$755,000	$270,000	$120,000	$85,000	$0
	Reducing Exposure to Indoor Air Pollution	$70,000	$0	$0	$300,000	$350,000
	Water Supply, Sanitation, and Hygiene	$0	$0	$0	$400,000	$475,000
	Urban Health	$0	$0	$0	$140,000	$25,000
	Total	**$1,475,000**	**$638,000**	**$758,000**	**$2,189,350**	**$2,168,000**
Health Systems Strengthening[5]	Service Delivery (Approaches and Technologies)	$862,100	$2,202,200	$1,005,280	$2,959,000	$2,060,000
	Health Workforce	$896,900	$578,100	$622,950	$1,950,000	$2,545,333
	Information	$4,176,981	$3,696,524	$4,200,000	$6,121,000	$6,541,000
	Pharmaceuticals Management	$614,389	$564,187	$715,000	$945,000	$1,200,000
	Financing	$555,000	$912,000	$345,000	$1,688,701	$2,236,892
	Governance	$400,000	$410,000	$445,000	$655,000	$820,658
	Total	**$7,505,370**	**$8,363,011**	**$7,333,230**	**$14,318,701**	**$15,403,883**
	TOTAL Funding	**$127,623,970**	**$136,601,911**	**$141,815,540**	**$153,827,247**	**$157,780,963**

1 This report highlights approximately 80 percent of the total health-related research at USAID.

2 This is a reclassification of the category of research based on the new operational plan documentation process.

3,4 As described in the 2006 *Report to Congress: Health-Related Research and Development Activities at USAID*, research findings are currently being introduced into programs.

5 The projected FY 2006 funding figures previously published in the 2006 *Report to Congress: Health-Related Research and Development Activities at USAID* did not capture all health systems research activities. USAID uses the World Health Organization's internationally recognized framework of six core functions of a health system to guide its research portfolio. This framework builds on the four research products outlined in the 2006 *Report to Congress: Health-Related Research and Development Activities at USAID* and uses a more comprehensive list of products in order to capture progress in this area of work more completely.

6 Research on Emerging Pandemic Threats has been added to the 2006 *Report to Congress: Health-Related Research and Development Activities at USAID* strategy, reflecting a recognized need for the development of comprehensive aggressive disease detection and response capacities.

Addendum II: Key USAID Global Health Research and Introduction Partners

Abt Associates
Academy for Educational Development
Alliance for Health Policy and Systems Research
Alliance for Microbicide Development
Alliance Group (Malawi)
Al-Quds Nutrition and Health Research Institute
Bayer Schering Pharma
Becton, Dickinson and Company
Bill & Melinda Gates Foundation
Boston University
CAMI
Canadian International Development Agency
Catholic Relief Services
Center for the AIDS Program of Research in South Africa (CAPRISA)
ChildFund International
Christian Reformed World Relief Committee
Concern Worldwide
CONRAD
Constella
CORE Group
Crucell
Danida
Department of Health and Family Welfare (India)
Division of Reproductive Health (Kenya)
Elizabeth Glaser Pediatric AIDS Foundation
EngenderHealth
Eunice Kennedy Shriver National Institute of Child Health and Human Development
European Commission
Family Health International
Food for the Hungry
Foundation for Innovative New Diagnostics
Futures Group
GenVec, Inc.
Georgetown University, Institute for Reproductive Health
GH Tech
GlaxoSmithKline PLC
Global Alliance for Improved Nutrition
Global Alliance for TB Drug Development
Global Alliance for Vaccines and Immunizations
Global Campaign for Microbicides
Global Drug Facility
Global Fund to Fight AIDS, Tuberculosis and Malaria
Global Health Workforce Alliance
Global HIV Vaccine Enterprise
Green Light Committee
Harvard School of Public Health
Health and Family Welfare Centers (Bangladesh)
Health Metrics Network
Health Research Department of Ghana Health Service
HealthRight International
Helen Keller International
ICDDR,B (Bangladesh)
ICF Macro
International Aid
International AIDS Vaccine Initiative
International Centre for Diarrhoeal Disease Research, Bangladesh
International Clinical Epidemiology Network
International Confederation of Midwives
International Federation of Gynecology and Obstetrics
International Food Policy Research Institute
International Partnership for Microbicides
International Rescue Committee
International Union Against Tuberculosis and Lung Disease
IntraHealth International
Irish Aid
Jhpiego
John Snow, Inc.
Johns Hopkins University
Kenya Medical Research Institute
London School of Hygiene and Tropical Medicine
Malaria Research and Training Center
Management Sciences for Health
MasiMax Resources, Inc./RTI International/AIM Activity
Medicines for Malaria Venture
Merck & Co., Inc.
Meridian Group International, Inc.
Microbicides Research Working Group
Micronutrient Initiative
Ministry of Health (Mozambique)
Ministry of Health and Population (Nepal)
Ministry of Health/TRAC Plus, Malaria Unit (Rwanda)
Ministry of Population Welfare (Pakistan)
Miz-Hasab Research Center (Ethiopia)
Mother and Infant Research Activities (Nepal)
National Institute of Allergy and Infectious Diseases
National Institute of Statistics (Mozambique)
National Institutes of Health
National Institutes of Health, Office of AIDS Research
Nepali Technical Assistance Group
Open Society Institute
Organisation for Economic Co-operation and Development
PATH
Pathfinder International
Pfizer
Plan USA
Population Council
Population Services International
Save the Children

Save the Children/Saving Newborn Lives program
Schering AG
Schering-Plough
SRA International
Stop TB Partnership Working Groups
Swedish International Development Cooperation Agency
Synergy Project
The Partnership for Child Health Care, Inc./BASICS
Tufts University
U.K. Department for International Development
UNAIDS
UNFPA
UNICEF
University of Aberdeen (Scotland)
University of Alabama
University of Bamako (Mali)
University of California at Davis
University of Malawi
University of Maryland, Center for Vaccine Development
University of North Carolina at Chapel Hill
University of the Witwatersrand (South Africa)
University Research Co., LLC
USAID/Mozambique
USAID/Nepal
U.S. Centers for Disease Control and Prevention
U.S. Department of Defense
U.S. Department of Health and Human Services
U.S. Food and Drug Administration
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U.S. Naval Medical Research Center
U.S. Pharmacopeia Drug Quality and Information Program
U.S. President's Emergency Plan for AIDS Relief
Valid International
Walter Reed Army Institute of Research
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Wellcome Trust
WHO Special Programme for Research and Training in Tropical Diseases
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