



USAID
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Report to Congress

Health-Related Research and Development Activities at USAID

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



September | 2009

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Acronyms and Abbreviations

ACT	Artemisinin-based Combination Therapy
AMR	Antimicrobial Resistance
AMTSL	Active Management of the Third Stage of Labor
ARI	Acute Respiratory Infection
ARV	Antiretroviral
BCC	Behavior Change Communications
CBD	Community-based Distribution
CCM	Community Case Management
CDC	U.S. Centers for Disease Control and Prevention
CHV	Community Health Volunteers
CHW	Community Health Worker
CM	Community Midwives
CMAM	Community-based Management of Acute Malnutrition
CPR	Contraceptive Prevalence Rate
CSB	Corn/Soy Blended Flour
CSHGP	Child Survival and Health Grants Program
DHS	Demographic and Health Surveys
DOTS	Directly Observed Treatment, Short Course
DTK	Diarrhea Treatment Kit
EML	Essential Medicines List

ENC	Essential Newborn Care
FDA	U.S. Food and Drug Administration
FP	Family Planning
FY	Fiscal Year
GAPP	Global Action Plan for Prevention and Control of Pneumonia
GSK	GlaxoSmithKline Biologics
HAPSAT	HIV/AIDS Program Sustainability Analysis Tool
HRRD	Health-Related Research and Development Activities at USAID
HTSP	Healthy Timing and Spacing of Pregnancies
IAVI	International AIDS Vaccine Initiative
IMCI	Integrated Management of Childhood Illness
IRS	Indoor Residual Spraying
ITN	Insecticide-treated Net
KMC	Kangaroo Mother Care
LAC	Latin America and the Caribbean
LLIN	Long-lasting Insecticide-treated Net
MCH	Maternal and Child Health
MVDP	USAID Malaria Vaccine Development Program
MVI	Malaria Vaccine Initiative
NGO	Nongovernmental Organization
NHA	National Health Account

OFDA	Office of Foreign Disaster Assistance
ORS	Oral Rehydration Solution
ORT	Oral Rehydration Therapy
OVC	Orphans and Vulnerable Children
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PMI	President's Malaria Initiative
POU	Point-of-use
PPH	Postpartum Hemorrhage
PVO	Private and voluntary organization
R&D	Research and Development
RDT	Rapid Diagnostic Test
RUTF	Ready-to-use Therapeutic Food
SDM	Standard Days Method
STI	Sexually Transmitted Infection
SWEF	System-Wide Effects of the Global Fund
TB	Tuberculosis
UN	United Nations
USAID	U.S. Agency for International Development
WHO	World Health Organization

Executive Summary

Research allows the U.S. Agency for International Development (USAID) to develop, test, and refine new and improved tools, approaches, and interventions, contributing to programs and policies appropriate for addressing health-related concerns in developing countries and countries in transition. USAID applies a proactive strategy that seeks to accelerate the development and introduction of research products that, when implemented in programs, will improve the health status of infants, children, childbearing women, and families, as illustrated in the Pathway from Research to Field Implementation and Use (see diagram below).

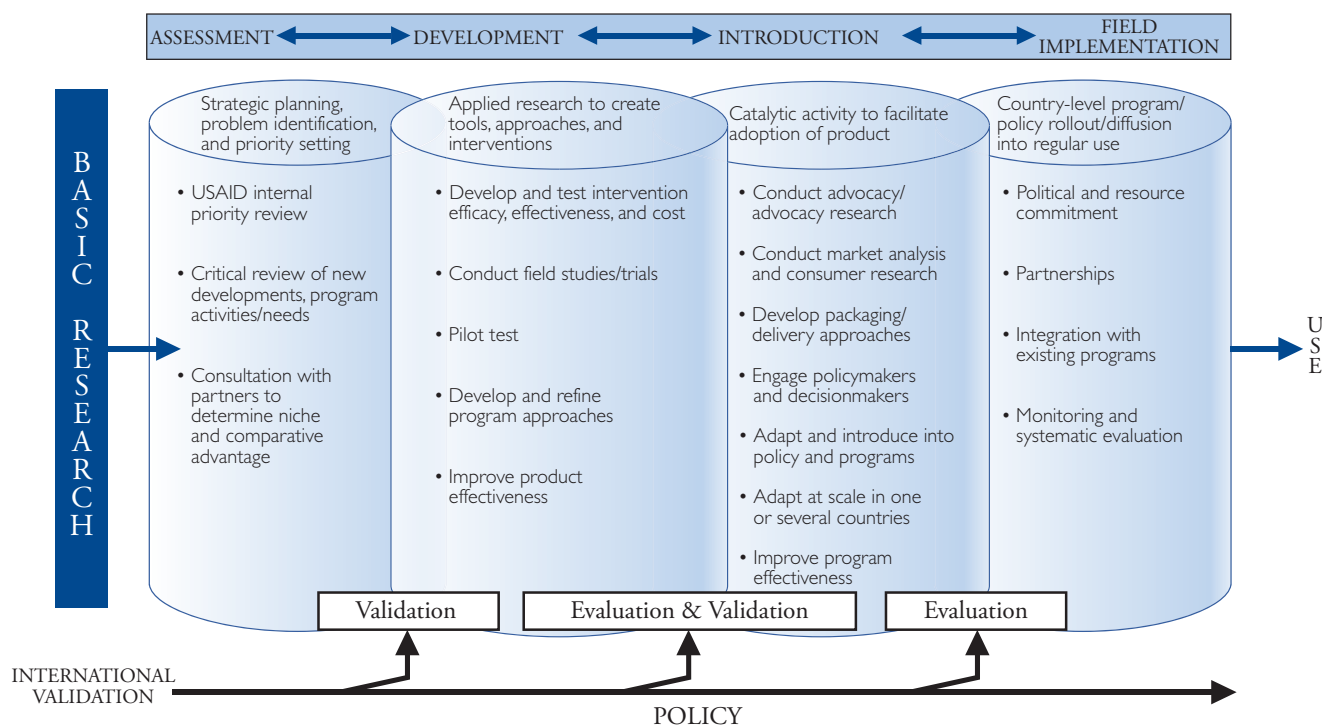
In 2006, USAID outlined its five-year health research strategy: *Report to Congress: Health-Related Research and Development Activities at USAID* (HRRD), May 2006¹. In 2008, USAID provided the first progress report, and this current report provides a further update on progress under this strategy for using research funds to stimulate the development and introduction of key products.

Over the last year, significant advances have been achieved in a number of areas, influencing policies and programming on the ground. Examples of achievements toward the goals of the five-year research strategy include the following:

- Strengthened the evidence base of the impact of ready-to-use supplementary foods (RUSF) on preventing chronic malnutrition. RUSF in Ghana and Malawi were found to prevent stunting, improve linear growth, reduce iron deficiency anemia, and enhance motor development in infants.
- Obtained regulatory approval for commercial marketing of Oxytocin-Uniject™. This single-dose injection is now available for use in field evaluations and pilot introduction efforts in community settings. This

¹ U.S. Agency for International Development. *Report to Congress: Health-Related Research and Development Activities at USAID*. May 2006.

Pathway from Research to Field Implementation and Use



Source: USAID

technology will simplify the prevention of postpartum hemorrhage (PPH) by community workers/midwives in community and lower level health care facilities.

- Advanced the introduction of the active management of the third stage of labor (AMTSL) – an evidence-based, low-cost intervention to PPH – in high-mortality countries. A USAID-supported multi-country survey of facility-based deliveries found limited practice of AMTSL. This has served as a strong advocacy tool to inform and influence policies and strategies for scaling up PPH prevention activities.
- Established the evidence base for home management of severe pneumonia. This new approach will reduce pressure on, and cost of, facility based care.
- Contributed to new joint World Health Organization (WHO) and UNICEF policy² based on USAID research investments endorsing community-based approaches to prevent and manage newborn illness through health worker home visits in a baby's first week of life.

The activities highlighted in this document represent approximately 80 percent (\$152 million) of the total amount USAID used in 2009 for the main areas of research on product development and introduction. This report does not cover an estimated \$38 million for research that is mainly funded by USAID field Missions on local questions and needs, such as formative research on child feeding practices, measurements of local disease burdens, or improvements in district health services.

The report reflects changes in the five-year health research strategy. A new chapter, *Child, Environmental, and Urban Health*, replaces the *Acute Respiratory Infections* (ARIs) chapter and highlights new activities related to ARIs, diarrhea therapy and prevention (previously outlined in the *Nutrition* chapter), and research on hygiene improvement interventions, indoor air pollution, and urban health.

Maternal and Newborn Health

The report leads with an update on maternal and newborn health research. An estimated 500,000 women die each year from complications of pregnancy and childbirth that could be prevented. Every minute, nearly 17 children under age 5 die – almost 8.8 million each year. Of these, 3.7 million are newborn infants who die with-

in their first month of life. Up to two-thirds of these deaths can be prevented if mothers and newborns received care from known, effective interventions.

USAID's Maternal and Child Health strategic approach³ is a reflection of its commitment to accelerate the development, introduction, and scale-up of the delivery of evidence-based interventions and integrated maternal, neonatal, and child health programmatic approaches in high-mortality countries. USAID supports research to accelerate the introduction and incorporation of morbidity and mortality reduction interventions into relevant community- and facility-based delivery programs for childbearing women and newborns.

- Studies in India and Pakistan have demonstrated the feasibility of community-based essential newborn care (ENC) in promoting neonatal health and survival. ENC includes basic preventive care practices, including clean delivery, promotion of breastfeeding, and treatment of newborn infection. In India, the use of ENC practices reduced neonatal mortality in the first month by 54 percent. In Pakistan, a community-based approach toward perinatal and postnatal ENC reduced neonatal mortality by about 15 percent and stillbirths by 20 percent.
- Research in Mali, supported by USAID, found midwives could safely administer oxytocin using Uniject™. Oxytocin-Uniject™ has the potential to increase the use of AMTSL by reducing logistic and programmatic barriers. Specifically, this simple, easy-to-use, single-use needle will not only simplify injections by midwives attending births in the community, but also will reduce policy barriers and concerns about misuse of needles outside of facility settings.
- A Bangladesh study showed that appropriate use and in-home delivery of misoprostol, a low-cost alternative to oxytocin, is associated with an estimated 40 percent reduction of immediate postpartum hemorrhage. Studies in Afghanistan and Nepal also demonstrated the safe and effective use of misoprostol.

2 WHO/UNICEF Joint Statement. Home Visits for the Newborn Child: A Strategy to Improve Survival, 2009.

3 U.S. Agency for International Development. *Report to Congress: Working Toward the Goal of Reducing Maternal and Child Mortality: USAID Programming and Response to FY09 Appropriations*. September 2009.

Child, Environmental, and Urban Health

Pneumonia and diarrhea are among the leading causes of preventable death for children under 5, accounting for 19 percent and 17 percent of preventable causes of young child mortality respectively. Ongoing research and introduction efforts build on proven approaches by investigating the management of non-severe and severe pneumonia in the community and facilitating the joint treatment of pneumonia and malaria, along with diarrhea – also known as community case management.

- An ongoing companion two-site study in Pakistan supported by USAID, in collaboration with WHO, is examining whether severe pneumonia can be safely treated at home after assessment by a cadre of government community health workers known as Lady Health Workers. If this study provides positive results, it will be possible to rapidly scale up this approach through the country's health system, as well as in other areas with low HIV prevalence rates. Further work will be needed to ensure the treatment is appropriate for areas with high HIV prevalence.
- Studies in Mali, Pakistan, and India advanced the evidence base on the use of zinc for management of diarrhea. In Mali, the promotion of zinc for diarrhea significantly increased oral rehydration solution (ORS) use and decreased antibiotic use. An effectiveness trial in Pakistan demonstrated that it is feasible to introduce zinc for the treatment of diarrhea in health systems at scale through community health workers. A study in India found that diarrhea is more effectively treated when caregivers receive education on zinc treatment and have ready access to supplies of ORS and zinc. Building upon the results of this research, all three country governments are positioned to begin large-scale implementation of zinc for diarrhea management.
- USAID-supported research on water testing technologies identified two simple, portable tests for measuring contamination of drinking water with fecal bacteria that can be performed by the consumer or others. These tests have the potential to: 1) support community and household water management systems, 2) provide entrepreneurial opportunities, and 3) enable assessment of water quality in disaster areas where equipment and skilled personnel are lacking.

Nutrition

More than half of the 8.8 million child deaths worldwide each year are related to malnutrition. One-third of children in the developing world are chronically

malnourished, and 2 billion people suffer from micronutrient deficiencies. USAID's nutrition research strategy addresses vitamin A deficiency, iron anemia prevention and treatment packages, community-based management of acute malnutrition, and dietary quality and diversity.

- A USAID-supported study in Haiti demonstrated that age-based preventive targeting of food assistance and behavior change communications is more effective in reducing childhood undernutrition than targeting only underweight children. Based on the study, USAID partners are adopting the Office of Food for Peace's "Preventing Malnutrition in Children under Two Approach" for maternal and child health and nutrition programming.
- USAID-funded research in Bangladesh contributed new evidence that a dose of vitamin A in the first 48 to 72 hours of life reduces infant mortality by 20 percent in vitamin A-deficient settings in South Asia. Operations research on newborn vitamin A supplementation is now being conducted in Nepal and Bangladesh. Implemented with global partners such as the Micronutrient Initiative, these studies will determine the feasibility of distributing vitamin A to newborns in the context of safe delivery and newborn care.

Reproductive Health and Family Planning

Family planning reduces unintended pregnancy and consequently reduces abortion and child mortality, improves birth spacing, and enables couples to achieve their desired family size. The objective of USAID's contraceptive research program is to improve and expand family planning use through provision of new and improved contraceptive methods, including methods that also reduce the transmission of HIV and other sexually transmitted infections. USAID's operations research program improves the availability and effectiveness of family planning and integrated reproductive health care in developing countries.

- Research in India demonstrated a 150 percent increase over 18 months in the prevalence of modern birth spacing methods among new users in the area where the Standard Days Method (SDM) was introduced. Results from a similar study in Peru suggest that introducing SDM may have stopped a declining trend in its use. The results further suggest that SDM is most popular among women who are not currently using an effective method, thus providing a strategy to reach underserved women and men.

- In an intervention to integrate maternal health, neonatal health, and family planning services in Kenya, more than 10,900 women received immediate postpartum visits that included postpartum family planning counseling. In the intervention group, 220 postpartum women started using family planning much earlier, and no pregnancies occurred at six months postpartum, compared with six pregnancies in 173 women in the pre-intervention group. At the six-week visit, significantly more women chose a contraceptive method after the intervention than before the intervention (63 versus 35 percent, respectively). The success of this intervention is widely acknowledged in Kenya, which plans to scale up integrated postnatal care/family planning services nationally.
- Enrollment in the USAID-supported, large-scale effectiveness study of the NES/EE contraceptive vaginal ring, conducted by the Population Council in collaboration with WHO and the National Institutes of Health, has been completed at 27 sites throughout the United States, Latin America, Australia, and Europe. Preliminary results indicate good contraceptive effectiveness and minimal side effects.
- IAVI's continued efforts to identify naturally occurring antibodies capable of blocking a wide variety of HIV has recently yielded noteworthy findings that are already providing very promising clues for vaccine development.

Malaria

Malaria remains one of the major causes of illness and death among children in Africa and is estimated to account for 300 million to 500 million illnesses and nearly 1 million deaths each year. USAID focuses on vaccine and drug development research, in concert with other global development efforts, to accelerate the availability of affordable and appropriate treatments for developing countries. USAID's Malaria Vaccine Development Program (MVDP) operates in the context of the worldwide malaria vaccine development effort, with a particular focus on vaccines for residents of malaria-endemic areas, primarily children and pregnant women. USAID supports the discovery and development of new antimalarial drugs and drug formulations, especially those that will be affordable to populations living in endemic areas. Operational and field research is supported that lays the groundwork for the safe and effective use of existing and new antimalarial drugs and drug combinations by national malaria control programs.

- MVDP, in collaboration with the U.S. Military's Malaria Vaccine Research and Development Program, completed two clinical malaria vaccine trials, began two trials (including a field trial in Kenya), and initiated preclinical work on a new vaccine concept. Working with the National Institute of Allergy and Infectious Diseases, a consultation on "The Rational Design of Malaria Vaccines" engendered new directions for the federal vaccine effort and for vaccine developers worldwide.

HIV/AIDS

An estimated 2.7 million new HIV infections occur every year, and no cure is available. Infected persons worldwide number nearly 33 million, and in sub-Saharan Africa, almost 60 percent of infected individuals are women. The International AIDS Vaccine Initiative (IAVI), a nonprofit organization, acts as a virtual pharmaceutical company. Biomedical research is undertaken in all phases of HIV vaccine clinical research and development, as well as other activities pivotal to advance research and development. USAID has promoted the development of microbicides, a class of health products to provide women with an effective chemical barrier to sexually transmitted HIV. This work focuses on the advanced testing of the most promising candidates available.

- IAVI, supported by USAID, the U.S. Centers for Disease Control and Prevention (CDC), and the U.S. Military HIV Research Program, provided key data to define laboratory values critical for designing and monitoring clinical trials, particularly trials of potentially lifesaving technologies, among African populations. The blood chemistry and hematology parameters of more than 2,000 people in Kenya, Uganda, Rwanda, and Zambia were examined, as were more than 20 parameters to evaluate kidney and liver functions, immunological health, and anemia.

Tuberculosis

Tuberculosis (TB) is one of the world's deadliest infectious diseases, with an estimated 9.2 million new cases and approximately 1.5 million deaths each year. Developing countries account for 95 percent of all TB cases and 98 percent of all TB deaths worldwide. USAID invests in research that will improve the performance and public health impact of country-level TB programs while mitigating the risks of drug resistance.

- USAID collaboratively supported the research and translation of evidence into global policy for the procedural shift from three to two smears in diagnosing TB. This policy change has the potential to increase case

detection rates while reducing the burden on both patients and laboratories of conducting multiple tests.

- A USAID-supported trial determined that fixed-dose combination tablets of TB drugs do not contribute to drug resistance, but it found some operational constraints to their use. For example, patients taking these drugs often have to interrupt treatment because they must stop all drugs if they have a reaction to just one.

Health Systems Strengthening

USAID works to strengthen health systems, be it through health- or disease-specific programs, across multiple health areas or across the whole system. USAID advances research in the six core functions, or building blocks, of a working health system, namely service delivery; human resources; information; medical supplies,

vaccines, and technology; health financing; and governance and leadership. USAID looks for constraints in quality, accessibility, or affordability and develops interventions within the framework of the six building blocks to address challenges and gaps.

- USAID established or strengthened post-marketing surveillance to sample and test the quality of medicines in Latin America, Africa, and Southeast Asia. USAID supported the sampling of approximately 900 antimalarials, TB and HIV/AIDS drugs, and antibiotics in Bolivia, Brazil, Guyana, Suriname, Paraguay, Peru, Vietnam, Laos, Cambodia, Philippines, Senegal, and Madagascar. Post-marketing surveillance data were instrumental in the success of a regional anti-counterfeit operation in Southeast Asia that led to the withdrawal of \$6.7 million worth of spurious medicines.

Partner countries referenced in this report include:

Afghanistan	Democratic Republic of the Congo	Kenya	Rwanda
Albania	Dominican Republic	Laos	Senegal
Angola	Egypt	Madagascar	South Africa
Argentina	El Salvador	Malawi	Suriname
Bangladesh	Ethiopia	Mali	Tanzania
Benin	Ghana	Namibia	Thailand
Bolivia	Guatemala	Nepal	Uganda
Botswana	Guinea	Nicaragua	Ukraine
Brazil	Guyana	Niger	USA
Burkina Faso	Haiti	Nigeria	Vietnam
Burundi	Honduras	Pakistan	Yemen
Cambodia	India	Paraguay	Zambia
Cameroon	Indonesia	Peru	
Cote d'Ivoire		Philippines	

Maternal and Newborn Health

Issues and Rationale

An estimated 500,000 women die each year from complications of pregnancy and childbirth that could be prevented. Every minute, nearly 17 children under 5 die – almost 8.8 million each year. Of these, 3.7 million are newborn infants who die within their first month of life. Up to two-thirds of these deaths can be prevented if mothers and newborns received care from known, effective interventions.

Mortality rates for mothers and children under 5 years of age remain alarmingly high in sub-Saharan Africa, where an African woman's lifetime risk of dying from pregnancy and childbirth-related conditions is 1 in 22, compared with 1 in 8,000 in industrialized countries. In most countries in Asia, maternal and child health has not kept pace with economic growth. Postpartum hemorrhage remains the biggest killer of childbearing women, and neonatal mortality has become a significant portion of child-related mortality. Most neonatal deaths are caused directly by infections, preterm births, and asphyxia. Low birthweight is the most important indirect cause of death, with 60 to 80 percent of neonatal deaths occurring among newborns who are born too small.

Areas of Research and Introduction

USAID develops and tests innovative approaches to achieve improved outcomes and reduce mortality and morbidity of childbearing women and newborns through community- and facility-based delivery programs. With systematic reviews of evidence to target investment in research and introduction activities, USAID will accelerate the testing and introduction of feasible prevention and management interventions for the main causes of maternal and newborn deaths.

Healthy Timing and Spacing of Pregnancies and Birth Outcomes

USAID has launched a wide range of activities and studies to help women and families ensure that pregnancy occurs at the healthiest times of a woman's life. Fifty-five to 70 percent of pregnancies in developing countries are spaced at too-short intervals, while 30 to 50 percent of girls experience their first pregnancy between the ages of 14 and 17 years. Under the Healthy Timing and Spacing

of Pregnancies (HTSP) initiative, USAID study findings have helped clarify and expand guidance to programs, provide new data to decision-makers on the role of family planning in maternal and newborn health, and expand information in pre- and in-service education materials.

USAID studies have shown that when pregnancies occur at the healthiest times of a woman's life, maternal and child survival are greatly increased. The studies indicate that early age, late age, and too closely and too widely spaced pregnancies are associated with high risks for the mother and child. These risks may include maternal, newborn, infant, child, and under-5 mortality; low birthweight and preterm birth; infant/child malnutrition; stillbirth; miscarriage; induced abortion; pre-eclampsia; and maternal morbidity (Figures 1 and 2). USAID-supported research has shown that a child born three to five years after the birth of a sibling is about 2.5 times more likely to survive than children born at shorter intervals, and less likely to be malnourished during infancy through age 5.

In 2008, USAID supported research in Egypt, India, Bangladesh, and Nepal to examine whether the addition of information on HTSP to client counseling increases the use of family planning for healthy pregnancy spacing. All four studies show that when families understand that modern contraceptive methods can be used to space births and improve pregnancy outcomes and child survival rates, family planning use increases significantly compared to control groups, regardless of income or cultural context.

USAID is examining the extent to which too-closely spaced pregnancies are associated with adverse child health outcomes. A USAID analysis of Demographic and Health Survey data, with a sample size of more than 1 million cases, found that birth-to-pregnancy intervals fewer than 36 months apart are associated with a statistically significant risk of under-5 mortality, stunting, and underweight. A separate study in Bangladesh identified maternal education and spacing of pregnancies as the two leading factors related to child mortality. The study found an increasing decline in mortality, from 2.3 percent in the early neonatal period to an estimated 16 percent in the childhood period, in relation to improvements in pregnancy spacing.

Maternal and Newborn Health Research Strategy 2006–2010

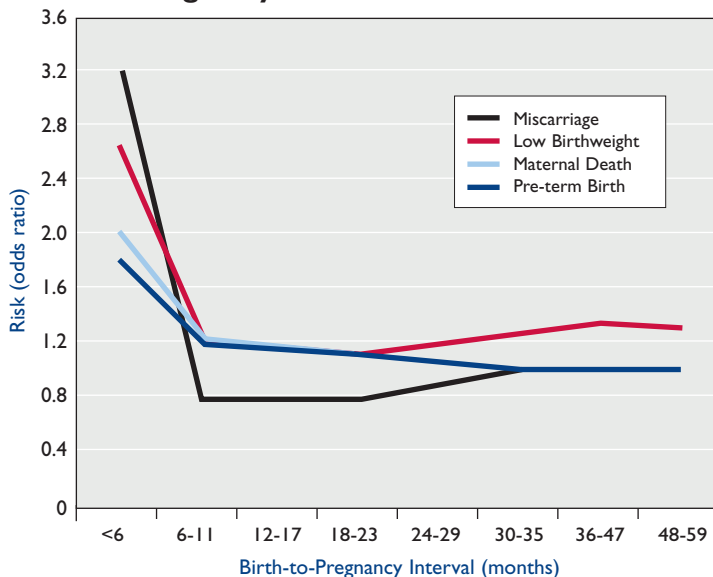
Total FY09: \$8,445,886	
Strategy Themes	Areas of Research and Introduction: Five-Year Strategy
Healthy Pregnancy and Birth Outcomes	Determine the health impact of Healthy Timing and Spacing of Pregnancies
	Develop and support the implementation of effective communication, education, and service delivery activities for Healthy Timing and Spacing of Pregnancies
Assessment of Birth Care and Outcomes	Impact of Cesarean section on birth outcome
	Global systematic review of direct causes of maternal mortality
	Review of physical, psychological, and economic consequences
	Impact of family planning in different settings on maternal mortality
	Evaluation of effectiveness and cost-effectiveness of approaches
Maternal Mortality Measurement Tools	Sampling at Service Sites to measure population-based maternal mortality
	Rapid Assessment Process for Maternal Death (RAPID) to measure maternal mortality in facilities
	Refine and validate Verbal Autopsy (InterVA-M) tool and apply in two to three countries
New Pregnancy and Birth Interventions and Introduction	Oxytocin-Uniject™: Conduct stability studies, scale up production, launch in multiple countries
	Active Management of the Third Stage of Labor: Apply at scale and measure coverage in five countries
	Determinants of postoperative fistula repair practices
	Pre-eclampsia and eclampsia: Develop and introduce evidence-based approaches
Neonatal Research and Newborn Care Practices	Essential Newborn Care: Complete effectiveness and cost-effectiveness studies and implement and evaluate minimal package of essential care
	Treatment and prevention of infections: effectiveness and cost-effectiveness studies, alternative formulations, and delivery strategies
	Strategies for care of low-birthweight infants: Evaluate and implement coordinated kangaroo care in facility- and community-level care
	Resuscitation device availability: Work with manufacturers to produce and distribute low-cost devices

To address young adolescent pregnancy, USAID is undertaking pilot studies to advance understanding of the causes of child marriage. Child marriage is linked to early pregnancy and increases the mortality and morbidity risk for mother and child. A USAID study in Ethiopia measured exposure to knowledge and skills surrounding child marriage prevention, documented the complex process of early marriage cancellation, and identified factors that shape health and social outcomes for girls whose marriages were stopped. In Yemen, where the legal age of marriage is 15 years, USAID is supporting a pilot study that examines the results of a “Safe Age of

Marriage” community education program. Findings from these studies will be used to strengthen child marriage prevention efforts.

USAID continues to build upon these findings to strengthen family planning, maternal and child health programs, and women-centered care. USAID is supporting eight new studies to advance understanding of age, pregnancy intervals, and health outcomes. In addition, a USAID partner will test an approach to identify high-risk pregnancies and ensure that these women receive appropriate services to reduce mortality risk. This

Figure 1: Birth-to-Pregnancy Intervals and Relative Risk of Adverse Maternal, Perinatal, and Pregnancy Outcomes

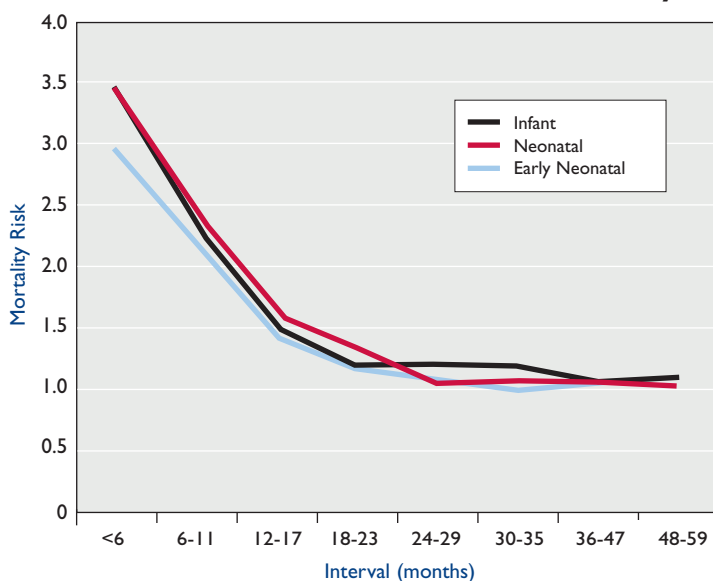


Source: Conde-Agudelo A, Belizán JM. Maternal morbidity and mortality associated with interpregnancy interval: cross sectional study. *BMJ*. 2000 Nov 18;32:1255-9.

Conde-Agudelo et al. "Birth spacing and the risk of adverse perinatal outcomes: a meta-analysis. *JAMA*. 2006 April 19;295(15):1809-23.

DaVanzo et al. Effects of interpregnancy interval and outcome of the preceding pregnancy on pregnancy outcomes in Matlab Bangladesh. *BJoB*. 2007 Sep.114:1079-87.

Figure 2: Birth-to-Pregnancy Intervals and Relative Risk of Neonatal and Infant Mortality



Source: Rutstein, S. Further evidence of the effect of the preceding birth intervals on neonatal infant and under-five mortality and nutritional status in developing countries: evidence from the demographic and health survey. DHS Working Paper No. 43. 2008.

approach may facilitate the scaling-up of family planning/maternal, newborn, and child health services at lower cost while achieving greater impact.

Assessment of Birth Care and Outcomes

USAID supports ongoing surveys in seven countries in Africa and eight in Asia to document the relationships between modes of delivery, including Cesarean section, and birth outcomes. This research is yielding information on the burden of maternal and perinatal complications and deaths.

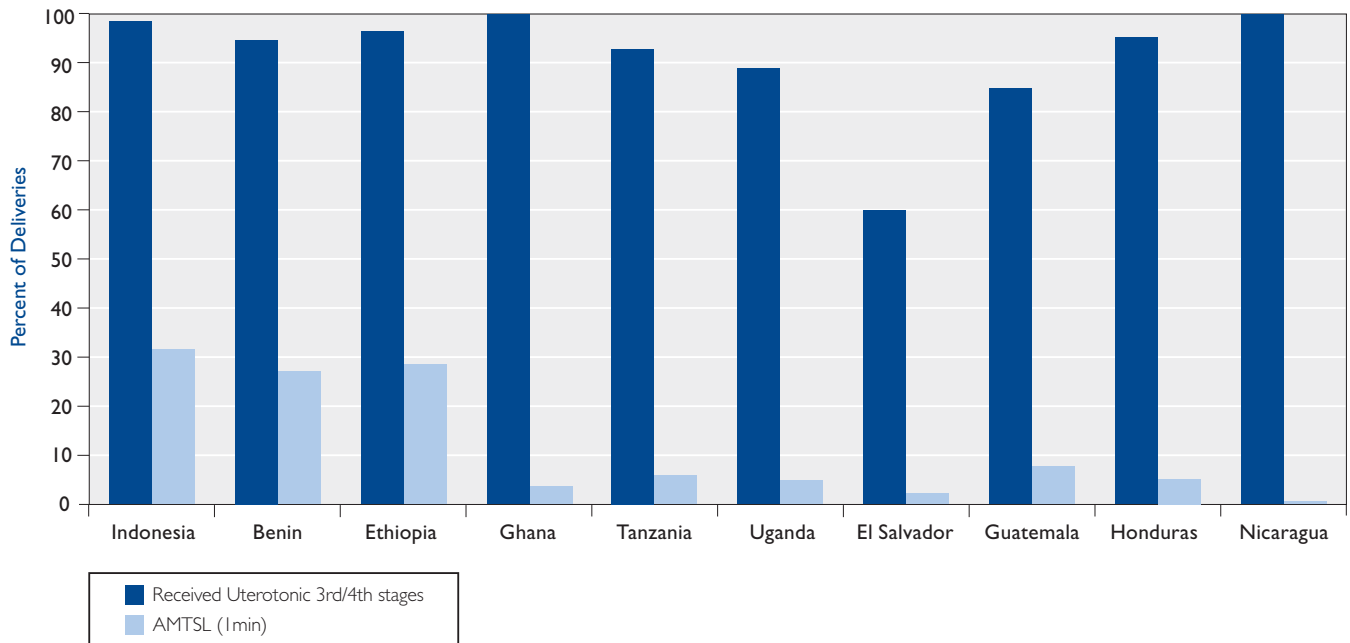
USAID is also supporting evaluation of promising health system innovations to reduce mortality. An analysis on the impact of Ghana's National Health Insurance program, which provides free antenatal and facility-based delivery care to insured women, supports the use of health insurance as a financing tool to reduce out-of-pocket expenditures for women seeking delivery care in health facilities, although premiums were found to act as a barrier to purchasing insurance. Since the completion of this analysis, all pregnant women have been exempted from paying premiums for enrollment. An evaluation of this new policy suggests that this approach can positively impact the poor and be cost-effective. A proposal to include family planning services and supplies in the benefit package is currently being considered. These policy changes will impact access to, and utilization of, maternal health services for women in Ghana and may inform other countries implementing a similar approach.

An ongoing USAID-supported study in Bangladesh will document the consequences of pregnancy-related morbidity, social and economic impacts of pregnancy-related complications, and risk factors for severe maternal pregnancy-related complications. Initial results indicate that women do not recognize the severity of long-term pregnancy-related complications and that there is a need for safe motherhood programs to prevent complications of pregnancy and increase access to emergency obstetric and gynecological care. The Bangladesh study has been undertaken in conjunction with companion studies in Burkina Faso and India supported by other donors. The information from these studies will guide ministries of health, United Nations (UN) agencies, and donors in key areas and interventions to improve ongoing safe motherhood programs.

Maternal Mortality Measurement Tools

USAID supported the analysis and development of tools to better evaluate the impact of maternal health

Figure 3: Percent of Observed Deliveries with Uterotonic Drugs Given During 3rd/4th Stages of Labor and Correct Use of AMTSL (Uterotonic Administration within 1 min)



interventions. These include ways to measure maternal and perinatal mortality and morbidity, the quality of maternal health care, economic outcomes, and health systems factors.

Sampling at Service Sites is one of several promising, low-cost techniques to measure the rates of maternal mortality in the community and offers potential cost and time savings over traditional house-to-house surveys. Since the development of this type of sampling, activities have focused on enhancing this tool to adjust for possible selection bias, adapting the method to different field settings, as well as raising awareness of this method.

An analysis of severe acute maternal morbidity – cases in which women nearly died but survived a complication during pregnancy, childbirth, or postpartum, also known as “near miss” – proposed definitions and identification criteria of cases and standard measures for inclusion in monitoring and evaluating quality of care. This approach and definitions will be applied in a World Health Organization (WHO) multi-country survey of maternal near miss.

Additional analysis and guidance for countries are available online: www.impact-international.org/index.php?id=67&rop=60.

New Pregnancy and Birth Interventions and Introduction

Active Management of the Third Stage of Labor

Postpartum hemorrhage (PPH) is a leading cause of maternal deaths in low-income countries. A USAID-supported WHO systematic review found a 6 percent prevalence of PPH (>500ml) and a 2 percent prevalence of severe PPH (>1,000ml) with wide variations across regions. This information will help guide programs in measuring and estimating blood loss in childbirth and assessing forecasting of pharmaceuticals and commodities to treat PPH.

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 uterotonic drugs, uterine massage after delivery of the placenta, and controlled cord traction are used to reduce blood loss and transfusions. USAID is working with professional societies, researchers, UN agencies, and the private sector to safely and effectively introduce AMTSL in high-mortality countries.

Oxytocin is a common uterotonic drug used to control bleeding after childbirth. A multi-country survey of facility-based deliveries found that although oxytocin is generally used to reduce bleeding after childbirth, cor-

Spotlight: Moving Research to Practice

Through the Healthy Timing and Spacing of Pregnancies (HTSP) initiative, USAID moves research into practice by means of fostering advocacy, bringing data to decision-makers, providing community outreach and education, and improving counseling and provider training. In 2008, 50 organizations and programs in developing countries reported incorporating HTSP data messages and guidelines into their global and country programs. Seven countries (Angola, Sudan, Rwanda, Senegal, Peru, Yemen, and Guatemala) reported institutionalizing HTSP information into national health guidelines and training curricula. Twenty-nine countries reported integrating HTSP guidelines into health programs.

rect use of AMTSL occurred in no more than one-third of observed deliveries (Figure 3). It is estimated that 1.4 million deliveries each year do not receive correct AMTSL. The survey served as a strong advocacy tool to encourage ministries of health, international partners, and policymakers to ensure that safe motherhood guidelines and practices include AMTSL.

USAID is also advancing research to simplify AMTSL, undertaking product development on delivery mechanisms and determining the safest and most feasible strategies for introduction. 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, Philippines, Thailand, and Uganda. A central objective of this trial is to determine whether a simplified package of oxytocin 10 IU IM/IV is comparable to the full AMTSL package. If this study has positive results, a simplified AMTSL regimen would significantly reduce the complexity of training workers in health facilities and in the community.

A USAID-supported WHO analysis concluded that misoprostol (a potential low-cost alternative for prevention of PPH) provided by a health worker trained in its use should be considered when oxytocin is not available at the community level. Misoprostol is an effective uterotonic that does not require refrigeration and can be administered orally. USAID-supported studies evaluated the safety, acceptability, feasibility, and program effectiveness of misoprostol given to women by volunteer community health workers (CHWs) in home births and in health huts. A Bangladesh study had a 90 percent well-timed use of misoprostol in home deliveries, with an estimated 40 percent reduction of immediate PPH.

Studies in Afghanistan and Nepal demonstrated the safe, effective use of misoprostol for PPH prevention through timely distribution of drugs accompanied with health education, clear packaging, and the retrieval of unused drugs. USAID is supporting the evaluation of community-based approaches to using misoprostol to prevent PPH in home births and rural maternity locations in Senegal.

Oxytocin-Uniject™

Oxytocin-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. In 2008, Oxytocin-Uniject™ received its first regulatory approval for commercial marketing as a pharmaceutical product and is now available for use in field evaluations and pilot introduction efforts in community settings. Oxytocin-Uniject™ has the potential to increase the use of AMTSL by reducing logistic and programmatic barriers and could overcome limitations to access in the community due to facility-based care policies for injections. In Mali, the use of this device by *matrones* was found to be feasible, safe, and preferred to a standard syringe. Further studies are planned in Guatemala, Honduras, Nepal, and South Africa.

Fistula repair

Obstetric fistula, the result of obstructed labor and lack of emergency obstetrical care, is a leading cause of maternal death and disability. An ongoing prospective facility-based study is capturing the basic characteristics of obstetric fistulas in an examination of the determinants of post-operative outcomes of fistula repair surgery. The study involves 13 sites across six countries: Bangladesh, Guinea, Niger, Nigeria, Rwanda, and Uganda.

The study is determining predictors of complications and success of fistula repair surgery and examining the socio-structural factors associated with fistula. This information will be used to identify potential new areas of research and to develop an evidence-based classification system, essential for promoting the standardization of high-quality care.

A qualitative study of 40 surgeons across Africa and Asia identified current practices in the care and treatment of fistula in relation to the use of antibiotics before, during, and after surgery; the role of catheterization in fistula management; and management practices for patients with stress incontinence after fistula repair. This information will be used to inform the development of a randomized controlled clinical trial. In addition, USAID is supporting a study on indications for Cesarean deliv-

Spotlight: Research-to-Use Model – Assessing the Effectiveness and Feasibility of Neonatal Infection Prevention Using a 4 Percent Chlorhexidine Solution

Frequently, neonatal infections occur in the umbilical cord stump, and research has shown that topical cleansing of the cord with chlorhexidine, a low-cost, readily available antiseptic drug, may reduce the risk of neonatal death from these infections.

In rural Bangladesh, more than 90 percent of women deliver at home with only a birth attendant or family members in attendance; the overall neonatal mortality rate exceeds 36/1,000 live births. A USAID-supported study is assessing the effectiveness and feasibility of infection prevention in the community through an antiseptic wash for the umbilical cord using a 4 percent chlorhexidine solution. The umbilical cord care intervention is being implemented as part of a proven ENC package involving community health worker (CHW) home visits prior to and after birth.

Services are being delivered at the household level to a population of approximately 500,000 in Sylhet District in the northeastern part of the country. Between 12,000 and 13,000 newborn infants are delivered each year in Sylhet. This new study is testing whether a one-day or a seven-day application of chlorhexidine is required to achieve a mortality reduction documented in a prior study in Nepal. In the first week after birth, village CHWs visit the homes of all infants to cleanse the umbilical cord with a 4 percent chlorhexidine solution and provide ongoing messages on dry cord care. In addition to this, CHWs administer a set of birth assessment data collection forms and questionnaires in the home.

While this study is ongoing, USAID is supporting product development work with a Bangladeshi pharmaceutical company to develop an affordable 4 percent chlorhexidine solution. USAID is also supporting a parallel research effort to determine optimal packaging for this product as well as testing whether families will access and use the antiseptic if it is offered through health clinics and pharmacies as a stand-alone product and/or as part of a birth kit.

eries in health facilities and an evaluation of cost assessment tools for fistula treatment services.

Pre-eclampsia/eclampsia

USAID is undertaking a concerted research and introduction effort to reduce pre-eclampsia and eclampsia. When hemorrhage as a cause of maternal death declines, as it has in Latin America and the Caribbean (LAC), pre-eclampsia and eclampsia become the leading causes of maternal death, accounting for 26 percent of maternal deaths in the LAC region and 9 percent in Asia and Africa. The condition adversely affects the placenta, resulting in poor intrauterine growth and premature birth. The goal is to develop, introduce, and scale up an evidence-based, comprehensive package of interventions to prevent and manage pre-eclampsia and eclampsia, and to generate evidence on technical and operational issues to facilitate program implementation. USAID is supporting a WHO systematic review of the evidence on pre-eclampsia and eclampsia, a multi-country survey to assess the quality of pre-eclampsia and eclampsia care in hospitals, and a study to identify biomarkers for pre-eclampsia.

Neonatal Research and Newborn Care Practices

Essential Newborn Care

Studies in India, Pakistan, and Bangladesh have demonstrated the feasibility of community-based Essential Newborn Care (ENC) in promoting neonatal health and survival. In India, the use of ENC practices reduced neonatal mortality in the first month by 54 percent. In Pakistan, a community-based approach on perinatal and postnatal ENC reduced neonatal mortality by about 15 percent and stillbirths by 20 percent. The Government of Pakistan is working to expand the intervention beyond the study area. In Bangladesh, the use of skilled birth attendants in uncomplicated deliveries, a mother's knowledge of newborn complications, and the use of ENC accounted for a 32 percent mortality rate differential across three districts. The study trained community health workers to identify and manage newborns with infections using a simple diagnostic approach, leading to a 34 percent mortality reduction. Community health workers were effectively able to treat 42 percent of cases of newborn infections with injectable antibiotics. *The Lancet* awarded the 2008 publication of this study its paper of the year award in recognition of the potential impact of the intervention in reducing newborn mortality.

USAID is introducing simple health-promoting behavior and care practices in the postbirth period in 24 USAID partner countries. Bilateral programs and USAID-supported Child Survival and Health Grants Program (CSHGP) partners are testing ENC packages in different program contexts.

A WHO/UNICEF joint statement titled “Home Visits for the Newborn Child: A Strategy to Improve Survival,” released at the 2009 United Nations Economic and Social Council meeting on global health issues, provides critical new guidance on prevention and management approaches that can be delivered through home visits in a baby’s first week of life. This statement builds upon USAID and the Bill & Melinda Gates Foundation’s Saving Newborn Lives/Save the Children-supported research, technical input, and assistance.

Treatment and prevention of newborn infections

Of the 4 million neonatal deaths that occur globally each year, 99 percent are in low-income and middle-income countries. Approximately one-third of these deaths can be attributed to infections caused by birth in unhygienic conditions. A multi-country trial, supported by USAID in partnership with the Gates Foundation’s Saving Newborn Lives/Save the Children and WHO, is researching different combinations of oral and intramuscular antibiotic regimens for simplified treatment of newborn sepsis in the community. With study sites in Bangladesh and Pakistan, this trial is testing the safety and effectiveness of implementing treatment regimens in periphery facilities and the community and their acceptability to families in settings with weak health systems.

In parallel with these efforts, a study in Zambia is testing the effectiveness and safety of initial treatment of infection with oral antibiotics, followed by facilitated referral to health facilities for intramuscular antibiotic regimens. The completed studies will strengthen the evidence base on infection management in young infants in community-based settings, provide policy recommendations for global programs, and guide future research priorities.

USAID is supporting the developing of simplified antibiotic regimens. One such effort involving Oxytocin-Uniject™ is an effort to extend the accessibility and facilitate the administration by lower-level health workers of a commonly used antibiotic, gentamicin. A prefilled, non-reusable injection device could help ensure immediate delivery of gentamicin in peripheral health care settings and homes. Trained CHWs and traditional

Key Partners in Maternal and Newborn Health Research and Introduction

Abt Associates
Bill & Melinda Gates Foundation
Boston University
Concern Worldwide
CORE Group
European Commission
EngenderHealth
ICDDR,B (Bangladesh)
International Aid
International Confederation of Midwives
International Federation of Obstetricians and Gynecologists
International Research Committee
Jhpiego
Johns Hopkins University
National Institutes of Health
ORC/Macro
Partner government ministries of health
PATH
Saving Newborn Lives/Save the Children
Schering-Plough
The Futures Group
The Partnership for Child Health Care, Inc./BASICS
U.K. Department for International Development
University of Aberdeen (Scotland)
University Research Corporation
Wellcome Trust
World Health Organization
World Relief
Wyeth

birth attendants could administer Gentamicin-Uniject™ at the first sign of a neonatal infection along with complementary antibiotics. Gentamicin-Uniject™ is now available for small-scale piloting from a private collaborating manufacturer, and USAID is supporting a pilot study of the device in Nepal.

Strategies for care of low birthweight infants

Questions remain on strategies to manage care for low birthweight (< 2,500 gm) and premature newborns in low-resource settings. Kangaroo mother care (KMC), or skin-to-skin care, is a promising approach practiced in hospitals in developed and some developing countries. A study in India found that low birthweight is not always viewed by caregivers as a determinant of health. Mothers instead pay attention to other visible factors such as whether the infant is feeding and/or alert. Concurrent to the community research, this approach is being introduced into facility settings in USAID-supported programs in Rwanda, Nigeria, Malawi, Nepal, and Bangladesh. Subsequent studies will evaluate approaches to community-based kangaroo mother care.

Increasing availability of resuscitation devices

Birth asphyxia accounts for 23 percent of the estimated 4 million neonatal deaths annually. Reducing birth asphyxia requires neonatal resuscitation skills and appropriate technologies for health workers present at birth.

USAID continues to advocate for the availability and use of low-cost resuscitation devices, increasing the understanding and awareness of the availability and performance of neonatal resuscitators, and the availability of appropriate devices in low-resource settings. Market assessments were conducted in Southern and Western Africa to increase demand for affordable devices and facilitate procurement of lower-cost, high-quality devices.

A study on the effectiveness of low-cost resuscitation devices in the community has been completed in Zambia. This two-and-a-half-year, cluster-randomized study trained traditional birth attendants to manage birth asphyxia and provide initial treatment for possible neonatal sepsis, in addition to HIV testing and prevention of mother-to-child transmission. Results of this study are expected later this year and will provide vital information on community-based care and the importance of addressing birth asphyxia and strengthening distribution networks for high-quality, lower-cost resuscitation devices as a component to neonatal care.

Child, Environmental, and Urban Health

Issues and Rationale

Pneumonia and diarrhea are among the leading causes of preventable death for children under 5, accounting for 19 percent and 17 percent of preventable causes of young child mortality respectively. If implemented at scale, immunization combined with standard case management with antibiotics could avert most, if not all, pneumonia-related deaths. Even without immunization, most pneumonia- and diarrhea-related mortality can be eliminated through case management. Case management involves a health worker classifying suspected cases based on breathing rates and lower chest in-drawing, treating pneumonia with antibiotics, and referring severe pneumonia cases to health facilities, where possible. In

developing countries, namely in South Asia and sub-Saharan Africa, where most of the deaths occur, facility-based case management may be limited and of inconsistent quality.

In a number of focus countries, USAID assistance has provided technical support to government, nongovernmental organizations (NGOs), and other partners to demonstrate effective and feasible programs to strengthen facility care while also extending community-based treatment of pneumonia in areas of low access. In the coming years, the challenges for these countries will be to move beyond effective demonstration in limited sites to larger-scale community programs that can be imple-

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

Total FY09: \$2,164,350	
Strategy Themes	Areas of Research and Introduction: Five-Year Strategy
Community Treatment of Non-severe Pneumonia and Diarrhea	→ Conduct demonstration studies in selected countries
Community Treatment of Severe Pneumonia	→ Effectiveness studies of outpatient and community health worker treatment of severe pneumonia
Joint Treatment of Malaria and Pneumonia	→ Effectiveness studies on joint treatment with antibiotics and ACT
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
	→ Catalytic studies to identify and address the factors increasing diarrhea mortality and ORT
Water Supply, Sanitation, and Hygiene	→ Development of scalable approaches to improve hygiene behavior and provide clean drinking water
Reduction of Indoor Air Pollution	→ Development of 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

mented with sustained quality and effectiveness. For new focus countries, the remaining barriers to use of antibiotics by CHWs will require additional efforts by local partners as well as the international community to ensure that enabling policies, plans, and resources are in place to support introduction.

A significant portion of the burden of diarrhea is preventable through well-defined hygiene improvement interventions. Key interventions include ensuring safe drinking water at the point-of-use (POU); access to and use of sufficient quantities of water; effective handwashing with soap by children and their caregivers; and proper disposal of human feces in a latrine, toilet, or other sanitary facility. USAID is conducting operational research to determine how to effectively and efficiently implement proven, evidence-based approaches on water treatment and safe storage at POU, handwashing with soap, and sanitation promotion.

Nearly 3 billion people rely on solid fuels, wood, animal dung, agricultural residues, and coal for cooking and heating. Indoor air pollution, resulting from the burning of solid fuels on open fires or simple stoves within the home, is a major health threat, especially for women and children who spend many hours in proximity to the fire. Globally, the use of solid fuels is estimated to account for 1.6 million excess deaths annually, two-thirds of which occur in South Asia and sub-Saharan Africa.

In 1975, roughly 27 percent of people in the developing world lived in urban areas; this had grown to 40 percent in 2000, and estimates suggest that it will reach 56 percent by 2030. An estimated 30 percent of the poor now live in urban areas; this proportion is projected to reach 50 percent by 2035. Maternal and child health challenges among urban populations are diverse. Unlike the relatively homogeneous needs among rural populations, the poor, at-risk populations in cities live in slum clusters or dispersed areas, and identifying and reaching them requires innovative strategies.

Areas of Research and Introduction

Community Treatment of Pneumonia/Community Case Management

Studies have shown that non-severe pneumonia can be safely and effectively managed by CHWs. Using this evidence-based approach, USAID has been working to address program and policy barriers that have limited treatment for non-severe pneumonia. Most recently, USAID has focused on integrating community

approaches to jointly manage severe pneumonia as well as undertaking operations and introduction research facilitating the joint treatment of pneumonia, diarrhea, and malaria. This approach, also known as community case management (CCM), is a promising way to extend care and may be an area for future program evaluation.

USAID is supporting the introduction and expansion of CCM of non-severe pneumonia in 11 countries in sub-Saharan Africa, Latin America, and South Asia. Though focused on pneumonia treatment, integrated approaches to addressing diarrheal diseases, malnutrition, and malaria, i.e., where appropriate, have been included in the CCM model. Currently, CHWs treat non-complicated cases while referring severe cases of pneumonia to peripheral facilities. In the Democratic Republic of the Congo, where CCM has been implemented in 611 sites in 11 out of 12 provinces, 11 percent of all cases were treated for non-severe pneumonia. This work, undertaken in partnership with host governments, NGOs, and UN agencies, is anticipated to continue under USAID's maternal and child health programming.

The Global Action Plan for Prevention and Control of Pneumonia (GAPP) was developed in collaboration with WHO's departments of Immunization, Vaccines, and Biologicals; Nutrition for Health and Development; and Public Health and Environment and with UNICEF and others, including the PneumoADIP and the Hib Initiative. Experts conducted a systematic review of pneumonia prevention and management globally, the results of which were published in a special supplement of the WHO Bulletin. A CCM implementation task force, including USAID, UNICEF, WHO's Department of Child and Adolescent Health, Save the Children, and the International Rescue Committee, has been formed to promote CCM in priority countries.

Joint Treatment of Malaria and Acute Respiratory Infections

A USAID-supported study in Zambia assessed the ability of volunteer non-professional CHWs to safely and effectively use malaria rapid diagnostic tests (RDTs). The National Malaria Control Program had previously trained CHWs in community-based treatment of malaria using artemisinin-based combination therapy (ACT). CHWs were instructed to treat patients testing positive for malaria, while patients testing negative, or those suspected of having pneumonia, were referred to the nearest health center for further diagnosis by a professional health worker. Preliminary results show an improvement in CHWs' RDT use over time. These study results indi-

cate that, in areas with shortages of professional health workers, community volunteers can not only diagnose and treat malaria, but may also act as a point of referral for severe cases of pneumonia.

USAID is supporting a study in Zambia to determine the effectiveness, feasibility, and cost-effectiveness of using CHWs to manage malaria and pneumonia with the aid of RDTs in poor rural settings. This is one of the first studies of this kind, and the Zambian Ministry of Health is anticipated to use this study as evidence for policy change on the use of Coartem with RDTs and antibiotics at the community level by CHWs.

Diarrhea Management: A Return to Oral Rehydration Therapy

In 2004, WHO/UNICEF released a joint statement recommending zinc for the treatment of acute diarrhea along with oral rehydration therapy (ORT). In an effort to roll out the implementation of these recommendations, USAID has supported the revision of country-level diarrhea treatment policies and health worker training manuals to ensure priority countries integrate zinc into existing public health programs. Introduction trials in several countries have been completed, providing an understanding of how to increase the availability and uptake of zinc treatment in the public and private sectors.

In Mali, the promotion of zinc for diarrhea significantly increased the use of oral rehydration solution (ORS) and decreased antibiotic use. An effectiveness trial in Pakistan demonstrated that it is feasible to introduce zinc for the treatment of diarrhea in health systems at scale using CHWs. A study in India found that diarrhea is more effectively treated when caregivers receive education on zinc treatment and have ready access to supplies of ORS and zinc. Building upon the results of this research, all three country governments are strengthening their commitment to large-scale implementation of zinc for diarrhea management. Government policy has been adopted in Pakistan and India, where zinc supply has been approved as part of the Indian Rural Health Mission.

USAID-supported operations research in Uttar Pradesh, India, is determining the best strategies for ensuring that zinc treatment is available to the approximately 30 million children under 5 in the state. The study is identifying effective delivery strategies for reaching rural health providers, chemists, wholesalers, and caregivers with information on improved diarrhea treatment. Five delivery approaches are being tested to determine which

are scalable, sustainable, and cost-effective, and will increase the knowledge, prescription, and use of zinc with ORS to treat childhood diarrhea.

In Kenya, where the most recent Demographic and Health Surveys show a 32 percent decrease in ORT use, USAID supported a study looking at the treatment of childhood diarrhea by primary caregivers, health workers, and pharmacy workers, and at access to ORS at the community level and within health facilities. Differences in ORT use were associated with limited access to ORS, conflicting information on the appropriate treatment for diarrhea, and lack of health worker endorsement of ORT. The study demonstrated there is a need to substantially increase the availability of ORS through local pharmacies and shops, to ensure that health workers recommend ORS for every episode of watery diarrhea, and to empower caregivers to initiate lifesaving rehydration therapy at home for children with diarrhea prior to seeking care.

Community Treatment of Severe Pneumonia

A systematic review of a USAID-supported multicenter study in Pakistan documented the effectiveness of community-based treatment of severe pneumonia. It showed an equivalency between inpatient intravenous drug therapy and outpatient home therapy with high-dose amoxicillin. Based on this research, WHO modified its recommendations on effective outpatient management of severe pneumonia using oral amoxicillin in non-HIV-endemic areas. The new guidelines promise to save lives and reduce expenses and pressure on strained tertiary facilities.

A two-site study in Pakistan, supported by USAID in collaboration with WHO, is examining whether severe pneumonia can be safely treated at home after assessment by a cadre of government CHWs known as Lady Health Workers. If this study provides positive results, it will be possible to rapidly scale up this approach through the country's health systems as well as an important contribution to the CCM approach. As this study was conducted in areas with low HIV prevalence rates, USAID is currently exploring opportunities to conduct similar studies in an HIV-endemic area in Africa where prior research suggests an alternative strategy will be needed to treat severe pneumonia.

Water Supply, Sanitation, and Hygiene

Ensuring safe drinking water at the point-of-use (POU) at the household, is possible through existing low-cost

technologies. The effectiveness of POU treatment products – both filter and consumable-based – for preventing diarrhea is well established, and remain a cost-effective option for providing drinking water until households have access to a safe piped-water supply. However, there is a need to identify the most effective ways of delivering POU products to populations at risk in order to increase access, adoption, and consistent use. USAID is supporting research to: 1) characterize the public benefits of POU, 2) determine whether subsidized and/or free products can be effective as a marketing tool to support the launch of new products, and 3) assess how subsidization or targeted free distribution may affect the sustainability and the commercial viability of these products. This research will help establish the most effective strategy for marketing and distribution of products to maximize the public health impact of POU interventions.

In Cambodia, USAID-supported research on the biosand filter, a promising household water treatment technology, found that more than 87 percent of filters were still in use after eight years, with a 45 percent reduction in diarrheal disease. A simple on-site testing method is needed in remote areas of the world where unsafe sources of water are commonly used for household drinking water purposes, and facilities for routine water testing are lacking. Research on water testing technologies identified two simple, portable tests for measuring contamination of drinking water with fecal bacteria that can be performed by the consumer or others. These tests have the potential to: 1) support community and household water management systems, 2) provide entrepreneurial opportunities, and 3) enable assessment of water quality in disaster areas where equipment and skilled personnel are lacking.

Research has shown that handwashing with soap, when done properly and at critical times, is an effective way to prevent acute respiratory infections (ARIs), reducing the incidence of ARIs by up to 40 to 50 percent. USAID is supporting a pilot study on an intervention to improve hygiene by handwashing with ash in densely populated communities in Bangladesh. Ash is often used in Bangladesh for handwashing; it has also been found to be effective for reducing fecal contamination on hands. If ash is an effective substitute for soap, then it could be included in recommendations for general and respiratory-related hygiene practices.

Indoor Air Pollution

USAID is contributing to research on indoor air pollution to take advantage of emerging health impact data,

coupled with support for, and participation in, international policy dialogue. Studies are assessing the impact of interventions on the reduction of ARIs, characterizing constraints to scaling up programs, and analyzing market-based strategies to reach high-risk populations.

Research in Nepal is assessing the relationship between the use of improved stoves and the incidence of ARIs. Additionally, qualitative research is informing on incentives for families purchasing, and using, improved cookstoves. USAID is also undertaking a review of existing indoor air pollution control efforts to identify potential research opportunities to accelerate the process of identifying effective and scalable approaches.

Urban Health

Beginning in 2001, USAID has assessed urban health challenges and piloted appropriate responses through the USAID-supported Child Survival and Health Grants Program (CSHGP) in several countries, including Bangladesh, Haiti, India, and Indonesia. USAID is undertaking a concerted research effort to evaluate existing community-based maternal and child urban health programs. The goal is to identify effective strategies and establish best practices toward facilitating the expansion of these programs in priority countries.

The Child Survival and Health Grants Program

USAID's CSHGP supports U.S. private and voluntary organizations (PVOs), NGOs, and their local partners to leverage “what works” in community-oriented programming and to implement innovative and effective maternal, newborn and child health, nutrition, and infectious disease projects that measurably improve health and nutrition and contribute to the reduction of morbidity and mortality.

PVO/NGO grantees consistently make important contributions to scaling up high-impact interventions, strengthening health systems and policies, and ensuring sustainability by developing effective partnerships with, and building the capacities of, ministries of health, local NGOs, and communities. In 2008, CSHGP supported 57 projects through 41 U.S. PVOs/NGOs in 28 countries, in collaboration with ministries of health and local NGOs. CSHGP projects provide opportunities for conducting research as a part of implementation for testing and refining promising programmatic approaches for delivering high-impact health interventions to the most underserved populations. CSHGP projects also provide country-specific evidence for national policy and programs.

Country-level examples of research by CSHGP PVO/NGO partners conducted over the past year include:

Cameroon: Helen Keller International, in collaboration with PLAN USA and Population Services International, assessed the feasibility of introducing zinc for the treatment of diarrhea in children under 5 in Cameroon. Health facilities and community-based organizations were provided with 1,720 courses of zinc (10 dose, 20-mg zinc blister packs), in addition to ORS sachets, for distribution in diarrhea treatment kits (DTKs). Findings revealed successful community-based distribution of DTKs, counseling for diarrhea management, and client utilization, and recommended that in addition to DTKs being provided at health centers, they should also be made available through trained community-based organizations to ensure widespread access and coverage of diarrhea treatment. Following this study, the Ministry of Health added zinc to the list of essential drugs, initiated procurement of the first zinc stocks, and is working to include zinc provision in the Integrated Management of Childhood Illness (IMCI) protocols for treatment of diarrhea.

Bangladesh: Christian Reformed World Relief Committee, in collaboration with the Ministry of Health and Family Welfare (MoHFW), examined the

ability of community-selected, unpaid community health workers to successfully identify, treat, and refer childhood cases of diarrhea and pneumonia through CCM. These community health workers, also known as community health volunteers (CHVs), correctly diagnosed and treated diarrhea and/or pneumonia in 85 percent of the 225 cases managed. The findings from this study demonstrate the effectiveness and feasibility of integrating CCM by trained CHVs into national community-IMCI strategies. The MoHFW had agreed to continue supporting CCM activities by ensuring the necessary supply of drugs for pneumonia and improving the health information system for tracking and follow-up of childhood illnesses.

India: Operations research conducted by the Aga Khan Foundation assessed the effect of community health worker distribution of preventive iron supplementation and nutrition education in areas with high prevalence of iron deficiency anemia in children and adolescent girls. Over a period of three months, the prevalence of anemia significantly declined, from 78.2 to 64.2 percent, among children (6–35 months), and from 73.8 to 54.6 percent among adolescent girls (12–19 years).

Five awards made in fiscal year (FY) 2008 are initiating operations research that will contribute to the Global

Table 1: Child Survival and Health Grants Program Planned Research Activities

Country	Research Description	Contribution: Research-to-Use Model
Pakistan <i>Aga Khan Foundation</i>	Increasing access to skilled birth attendants through developing a cadre of community midwives and testing an NGO contracting model for replicating the nascent national community midwifery initiative in other remote, under-served districts.	Introduction
Afghanistan <i>World Vision</i>	Improving maternal health outcomes through piloting the use of telemedicine (i.e., cell phones) by CHWs and midwives in remote areas.	Introduction
Nicaragua <i>Catholic Relief Services</i>	Reducing delays and other barriers to care seeking for maternal and neonatal complications through a model of constructive male involvement.	Introduction
Nepal <i>Helen Keller International</i>	Assessing the added impact, cost-effectiveness, and potential for scale-up of implementing two proven strategies (Essential nutrition actions and Homestead food production) to address complementary, critical facets of malnutrition versus the strategies implemented alone.	Introduction
Burundi <i>Concern Worldwide</i>	Assessing the cost-effectiveness and potential for scale-up of a community-driven intervention model to effectively prevent stunting among young children in food-insecure settings.	Introduction

Health Bureau's Research-to-Use Model by addressing topics of national and global significance (Table 1).

PVO/NGO-led operations research contributes to advancing global leadership within USAID and the global agendas for maternal, neonatal and child health; nutrition; and malaria by demonstrating and scaling up NGO programming achievements. Awards made in FY09 are leveraging partnerships with local universities or research institutions to ensure strategic dissemination of results and uptake of successful programmatic innovations in country and continue to build in-country expertise on health operations research.

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

Aga Khan Foundation
Aga Khan University
Bill & Melinda Gates Foundation
Boston University
Catholic Relief Services
Christian Reformed World Relief Committee
Concern Worldwide
CORE Group
Helen Keller International
ICDDR,B (Bangladesh)
Jhpiego
Johns Hopkins University
Partner government ministries of health
PLAN USA
Population Services International
Save the Children
The Partnership for Child Health Care, Inc/BASICS
UNICEF
World Health Organization
World Relief
World Vision

Nutrition

Issues and Rationale

More than half of the 8.8 million child deaths worldwide each year are attributable to malnutrition. One-third of children in the developing world are chronically malnourished, and 2 billion people suffer from micronutrient deficiencies. Vitamin A deficiency affects more than 254 million children, impairing their immune systems and causing blindness, early morbidity, and mortality. Iron deficiency is one of the primary causes of anemia, which is responsible for 22 percent of maternal deaths and 24 percent of perinatal deaths.

USAID expands evidence-based approaches to nutrition and supports innovative new approaches for improving implementation and targeting of the most vulnerable populations. USAID’s comprehensive nutrition approach focuses on:

- Preventing malnutrition through a package of maternal, infant, and young child programs that focus on nutrition from conception to 2 years as a window of opportunity for intervention.
- Reducing micronutrient deficiencies through targeted supplementation to vulnerable groups and food fortification
- Strengthening community-level programs to manage acute malnutrition
- Improving nutritional outcomes in food security, humanitarian assistance, and HIV programs

USAID’s research-to-use nutrition strategy specifically addresses vitamin A deficiency prevention and control,

Nutrition Research Strategy 2006–2010

Total FY09: \$2,680,810	
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 identify and undertake priority research as appropriate
	Establish best practices for the increased coverage and implementation of reproductive health packages that 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 (CMAM)	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 (RUTF)
	Test alternative formulations of RUTF for cost and local effectiveness

anemia prevention and treatment, community management of acute malnutrition, and dietary quality and diversity. USAID-supported research on the use of zinc for the treatment of diarrhea is described in the *Child, Environmental, and Urban Health* chapter of this report.

Areas of Research and Introduction

Vitamin A Deficiency – Prevention and Control

USAID supported original research in the 1980s that showed a 23 percent reduction in child mortality when a child receives a high-dose vitamin A supplement twice a year. USAID continues this legacy by providing global leadership in scaling up and sustaining national vitamin A supplementation programs for children under 5. USAID research focuses on addressing barriers to achieving coverage and developing tools and strategies to transition programs to sustainable, government-managed programs. Based upon the findings from a USAID-funded multi-country study of logistics and financing of vitamin A supplementation programs that identified enhanced strategies to reach the most vulnerable populations, USAID is able to implement a management system that increases program coverage.

Recent USAID-funded research in Bangladesh contributed to a growing body of evidence that a newborn dose of vitamin A in the first 48 to 72 hours of life reduces infant mortality by 20 percent in high-mortality, vitamin A-deficient settings in South Asia. USAID is now translating these research findings to use by conducting operations research on newborn vitamin A supplementation in Nepal and Bangladesh. These studies, implemented in collaboration with global partners, such as the Micronutrient Initiative and UNICEF, will determine the feasibility of distributing vitamin A to newborns in the context of safe delivery and newborn care.

Anemia Prevention and Treatment Packages

Inadequate iron intake is one of the primary causes of anemia, a disease that is responsible for 22 percent of maternal deaths and 24 percent of perinatal deaths, and that irreversibly compromises cognitive development in children.

USAID is supporting operations research on best practices for increased coverage and implementation of maternal health packages that include anemia control and prevention. Research includes assessments of current gaps within the pharmaceutical supplies and logistics

Spotlight: Research-to-Use Model: A New Approach to Prevention of Malnutrition in Children under 2

Due to the increase in food prices from 2006 to 2008, food insecurity and malnutrition is on the rise in many developing countries. USAID's Global Health programs work with PL 480/Title II to target food-insecure and vulnerable regions of every country receiving U.S. food aid. A USAID-supported study in Haiti demonstrated that age-based preventive targeting of food assistance and behavior change communications is more effective in reducing childhood undernutrition than targeting only underweight children as part of nutrition programs for the most vulnerable. This new approach, which focuses on prevention rather than recuperation, was adopted as the recommended model for all Title II maternal, child health, and nutrition programming. USAID partners are adopting the "Preventing Malnutrition in Children under 2 Approach" for maternal and child health and nutrition programming based on the study.

system in Uganda and India to ensure supplies exist for effective programming.

Anemia and poor iron status in children robs vital organs of oxygen, resulting in poor performance of brain, immune, and muscle function and growth and development deficits that can be irreversible. Very few developing countries implement comprehensive child anemia prevention programs, and as a result, child anemia is over 70 percent in most of USAID's maternal and child health (MCH) priority countries.

In 2008, USAID conducted formative research and baseline studies in two states in India to guide design and implementation of child anemia programs. Findings showed that anemia affects more than two-thirds of young children and shows no signs of declining without intervention; that iron deficiency and worm prevalence are the two major factors in causality of anemia; and that infant and young child feeding practices are extremely poor and must be addressed alongside improved iron/micronutrient intakes.

Dietary Quality and Diversity

Infant and young child feeding is part of a continuum of critical nutrition and health practices that begins during pregnancy and continues through at least the first two years of life. A package of key interventions includes

maternal nutrition, immediate initiation and exclusive breastfeeding through the first six months of life, introduction of high-quality complementary foods at 6 months, age-appropriate complementary feeding practices, and safe and active feeding during and after illness. USAID's research strategy focuses on approaches to improve complementary foods, including enhancing the quality of complementary foods through micronutrient powders and lipid nutrient supplements and improving measurement of dietary adequacy.

USAID supported the original efficacy studies for micronutrient powders and is now supporting an effectiveness study in Cambodia. This study evaluates the effectiveness of providing infants 6 to 11 months of age with daily micronutrient powders – in addition to nutrition education targeted to caregivers to improve feeding practices – to reduce iron deficiency anemia as well as other micronutrient deficiencies and improve growth of children 6 to 23 months. Preliminary data from this community-based distribution system show that more than 90 percent of children consume micronutrient powders four to five times a week. USAID is also working with partners such as UNICEF to develop guidelines for the integration of micronutrient powders into national nutrition programs.

Lipid nutrient supplements are point-of-use supplements that contain micronutrients and essential fatty acids. These supplements have been shown to improve linear growth of children, prevent severe stunting, reduce iron deficiency anemia, and enhance cognitive and motor development when provided starting at 6 months of age. There is also growing evidence of the importance of essential fatty acid intake during pregnancy and lactation, with consequences for child neurological development and maternal health.

USAID is working with international and national partners to identify effective interventions and delivery mechanisms that can be implemented by national governments and the private sector at scale. USAID is building the evidence base through effectiveness trials on the impact of lipid nutrient supplements on:

- Prevention of chronic malnutrition. Protocol development is under way in two countries in Latin America and South Asia.
- Prevention of seasonal increases in acute malnutrition, implemented in collaboration with the Office of Foreign Disaster Assistance (OFDA) partners.

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
 UNICEF
 University of California at Davis
 University of Malawi
 U.S. Pharmacopeia Drug Quality and Information
 Valid International
 Washington University in St. Louis
 World Health Organization

- Integration into emergency food ration packages for prevention of acute malnutrition in vulnerable, disaster-affected populations, implemented in collaboration with OFDA and Food for Peace partners. In 2008, USAID and research partners completed a study of the impact of lipid nutrient supplements and corn/soy blended flour (CSB) on moderately wasted children. Results from this randomized clinical effectiveness trial found that moderately wasted children who received the supplements were more likely to recover than those who received CSB.

USAID is also working with the private sector to identify effective and sustainable production of lipid nutrient supplements and developing global guidelines for the integration of such supplements into national health and nutrition programs.

USAID supports mass food fortification programs in more than 20 countries and is supporting research to strengthen the design, implementation, and monitoring and evaluation of these programs. USAID collaborated with researchers to use household income and expenditure survey information to establish a feasible process to assess the need and potential benefit of mass fortification. Based on years of program experience, USAID supported the development of the Food Fortification Formulator, a tool designed to ensure safety and maximum efficacy of mass fortification programs. The Formulator is now used in more than 10 countries in Latin America and Africa.

Improving measurement of dietary adequacy and strengthening nutrition surveillance methods are critical to nutrition programs. In 2008, results from the USAID-supported Women's Dietary Diversity Project study in five countries indicated that food group diversity indicators are a simple and valid option for population-level assessment and for monitoring progress toward improved micronutrient intakes among women of reproductive age. USAID-supported partners also finalized a study on alternative sampling designs that identified accurate methods of measuring nutrition and food security status in emergencies that are less time-consuming and less expensive but equally as precise as the gold standard. The findings from both of these studies are now informing global guideline and indicator development to improve monitoring and evaluation of nutrition programs.

Community Management of Acute Malnutrition

Approximately 63 million children are acutely malnourished. Until recently, the management of acute malnutrition was limited to center-based care with limited

coverage. An approach pioneered by USAID and NGO partners, called Community-based Management of Acute Malnutrition (CMAM), brings the services for management of acute malnutrition closer to beneficiaries, thanks to the availability of ready-to-use therapeutic foods (RUTFs)⁴.

USAID supports CMAM research related to the integration of CMAM into national health systems, CMAM in post-emergency situations, national production of RUTFs, and tools for global CMAM training and planning. In 2008, USAID, other donors, and researchers came together to develop guidelines on integration of CMAM into national health system programs. This guidance was integrated into a study on CMAM integration in post-emergency contexts.

Two USAID-supported efficacy trials in Ghana and Malawi have strengthened the evidence base of the impact of RUTFs on preventing chronic malnutrition. RUTFs were provided to children for six to 12 months starting at 6 months of age. The RUTFs prevented stunting, and the children showed improved linear growth, reduced iron deficiency anemia, and enhanced motor development. In collaboration with a private sector partner, USAID completed a local RUTF production feasibility assessment in Ghana, and local production is anticipated to begin in 2009. These new products will be a critical component of USAID's efforts to improve nutrition in light of growing food insecurity.

4 World Health Program, United Nations System Standing Committee on Nutrition, and UNICEF. Community-based Management of Severe Acute Malnutrition: A Joint Statement by the World Health Organization, the World Food Programme, the United Nations Systems Standing Committee on Nutrition and the United Nations Children's Fund. May 2007.

Reproductive Health and Family Planning

Issues and Rationale

Family planning (FP) reduces unintended pregnancy and, consequently, reduces abortion and child mortality, improves birth spacing, and enables couples to achieve their desired family size. Thus, a wide range of contraceptive choices ultimately promotes maternal health and child survival.

In addition to the unmet need for contraceptives, nearly every developing country needs substantial improvements in coverage and quality of FP services and effective ways to reach out to youth, men, and the hard-to-reach rural poor. Access to services that can provide a

minimal range of contraceptive options, for example, is not available to 75 percent of individuals living in sub-Saharan African countries.

Areas of Research and Introduction

Contraceptive Research and Development Program

The objective of USAID's contraceptive research program is to improve and expand FP use through provision of new and improved contraceptive methods, including methods that also reduce the transmission of HIV and other sexually transmitted infections (STIs).

Reproductive Health and Family Planning Research Strategy 2006–2010

Total FY09: \$30,197,000	
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 MCH, HIV/AIDS, and other health services
	→ Assess cost efficiency of integrated services

Contraceptive research

Enrollment in the USAID-supported, large-scale effectiveness study of the NES/EE contraceptive vaginal ring, conducted in collaboration with WHO and the National Institutes of Health (NIH), has been completed at 27 sites throughout the United States, Latin America, Australia, and Europe. Preliminary results indicate good contraceptive effectiveness and minimal side effects. Once approved by the U.S. Food and Drug Administration (FDA), this one-year contraceptive method will fill the gap in FP methods between the three-month injectable and the five-year implant.

A large-scale contraceptive effectiveness and safety study of the SILCS diaphragm, a “one-size-fits-most” reusable barrier method, is being conducted in eight sites across the United States, with USAID support. Once approved by the FDA for contraceptive use, additional studies will be undertaken to determine its effectiveness in reducing STI transmission, as well as develop instructions needed to be able to provide this method without a prescription.

With the trial currently under way, USAID’s partners are laying the groundwork for commercialization by identifying private sector manufacturing partners, evaluating the market and distribution channels for SILCS, determining the technical feasibility of using SILCS as a microbicide delivery system, and assessing regulatory and commercialization implications of over-the-counter distribution.

The Woman’s Condom is a proven technology that improves reproductive health and protects against sexually transmitted infections. PATH has completed the due diligence process and identified a manufacturing partner for the Woman’s Condom, a product developed with USAID support. With a commercial supply from this partner, PATH will be able to perform clinical trials for regulatory approval by the FDA and other stringent regulatory authorities.

Improving and expanding the use of contraceptive methods and services

Developed by USAID-supported researchers, the Standard Days Method (SDM) helps couples to recognize when they are most fertile and avoid unprotected sex during fertile periods of the menstrual cycle. USAID-supported research in India demonstrated a statistically significant increase – 150 percent over 18 months – in the prevalence of modern birth spacing methods among new users in the area where the SDM was introduced compared to a control area (41 percent). Results from a similar study in Peru found a 32 percent increase among new users compared to a 9 percent

decrease in the control area. These results indicate that introducing the SDM will neither displace nor negatively affect established FP methods and suggest that the SDM is most popular among women who are not currently using an effective method, thus providing a strategy to reach underserved women and men.

Building on USAID-supported safety and feasibility studies of community-based distribution (CBD) of injectable contraceptives, scale-up activities are now taking place throughout sub-Saharan Africa. Kenya, Nigeria, Rwanda, and Tanzania conducted educational tours of the program in Uganda, where CBD of injectables has been implemented in the districts of Kanungu, Mubende, Bugiri, and Busia. Plans are moving forward for the introduction and scale-up of this approach in Kenya; Nigeria and Rwanda are both committed to developing national plans for the introduction of this practice.

Family Planning Operations Research

The objective of USAID’s Operations Research program is to improve the availability and effectiveness of family planning and integrated reproductive health care in developing countries. This objective is achieved through assessing the needs and gaps in existing programs, developing new program and service delivery approaches to address these gaps, developing tools and materials to improve provider performance, and improving the capacity of communications and behavior change programs to increase client awareness and use of existing services.

Improving approaches to address unmet need for family planning services of underserved groups

In Egypt, USAID supported research on behavior change communication (BCC) interventions to improve birth spacing intervals that were given during pregnancy, immediately after delivery, and through contact several times postpartum. Contraceptive use at 10 to 11 months postpartum was significantly higher in the intervention area (48 percent versus 31 percent), and those women used contraception for a much longer time during the postpartum period (seven months versus three months). In Kenya, USAID supported the development of a three-day training curriculum and revised postnatal schedule, with a particular focus on FP, leading to an improvement in provider knowledge and the quality of client counseling. Women using FP were more likely to start by two months postpartum (62 percent versus 6 percent), and fewer women had an unmet need at six months or had become pregnant. Women and their infants attended postnatal clinics earlier and more frequently in the six months postpartum.

Spotlight: Increasing Access to Family Planning Services in Albania

The American Red Cross (ARC) and the Albanian Red Cross (AlbRC), funded by the USAID Child Survival and Health Grants Program (CSHGP), partnered to successfully increase access to family planning information and counseling and to expand the method mix in Diber Prefecture.

Baseline surveys in 2003 revealed a 9 percent contraceptive prevalence rate (CPR) in Diber and a 94 percent unmet need for modern family planning methods. Among married couples, 67 and 74 percent of women and men, respectively, relied on withdrawal methods, citing fear of side effects, partner preference, and insufficient knowledge as reasons for not using modern contraception. Prior to project activities, FP services in Diber were only available at health centers at the commune level.

The project successfully advocated for the Ministry of Health (MOH) to expand FP services to 42 village health posts in the three project districts. Project staff trained 277 village nurse-midwives in FP counseling and included FP in the Community-integrated Management of Childhood Illness training for all 600 village health team members. Among women of reproductive age, the project recorded a more than two-fold increase in modern contraceptive use, from 9 to 22 percent, and an increase from 20 to 87 percent in those who reported discussing FP with a health worker or promoter in the previous 12 months over the period 2004–2008.

In addition, ARC and AlbRC introduced the Standard Days Method (SDM) in country, in partnership with Georgetown University's Institute for Reproductive Health Project and the MOH. Staff trained 89 health providers in 25 health centers in three districts on the use of SDM. This method was incorporated into the method mix and offered alongside other MOH-approved methods during health education and counseling sessions. Project findings revealed that among 254 women in three districts who chose a modern method to fulfill their stated interest in both spacing pregnancies or limiting family size, SDM (30 percent) was the second-most popular method, after oral contraceptives (44 percent), and the method helped increase the number of new users of family planning.

The study results show that women chose SDM because they experienced that it had no side effects. SDM was found to be easily understood by both provider and client, and only one case of client method failure was recorded. These findings led the MOH to officially approve SDM for general use, thereby expanding the available FP method mix.

A USAID-supported study demonstrated the feasibility and acceptability of offering reproductive health services at the women-focused Health and Family Welfare Centers in Bangladesh. The Bangladesh MOH has implemented this model in 40 centers across four districts. The addition of these services for men, which included FP, condom use, and STI treatment, led to a 30 percent increase in the client load over six months, with 17 percent of adult clients being men.

Improving integration of family planning and other health care services

Systematic screening is a simple checklist tool that is effective for improving the integration of clinical maternal and child health and FP services and increasing provider productivity. USAID supported the development of a training manual to provide guidance on the integration of systematic screening in health facilities to increase the proportion of clients receiving multiple services in a single visit. Client needs are first identified and may then be provided in a single visit or through referral

to a separate facility, if required. Seven studies in five countries provided evidence that the tool improves the number of services received per client visit by up to 28 percent. Based on this finding, systematic screening is considered a "best practice" and is being scaled up in Senegal and India, and introduced in Bangladesh, Rwanda, the Philippines, and Madagascar.

An integrated postnatal care-FP model, developed in Kenya with USAID support, has demonstrated promise as an effective approach to integrating maternal and neonatal health and FP services. In the intervention group, 220 postpartum women started using FP much earlier, and no pregnancies occurred at six months postpartum compared with six pregnancies in 173 women in the pre-intervention group. At the six-week visit, significantly more women chose a contraceptive method after the intervention than before the intervention (63 percent and 35 percent, respectively). More than 10,900 women have received immediate postpartum visits, which include postpartum FP counseling. The success of

this intervention is widely acknowledged in Kenya, which plans to scale up integrated postnatal care/FP services nationally.

The Balanced Counseling Strategy, developed with USAID support, is a set of a practical, interactive counseling tools that incorporate current FP norms and guidance as recommended by WHO and USAID. The process, tested and refined in several countries, involves a set of steps to determine the method that best suits the client according to her preferences and reproductive health intentions. More than 14,000 requests for hard copies in English, 5,000 in Spanish, and 1,500 in French have been received. With support from the U.S. President's Emergency Plan for AIDS Relief, a BCS-Plus has been adapted for use in high STI/HIV prevalence settings, and systematic evaluations in African countries have proven the tool effective in significantly increasing STI/HIV preventive behaviors among FP clients, including dual protection and HIV testing.

A USAID project has successfully demonstrated the implementation of a community-based package of safe motherhood services that includes postpartum FP in Kenya. This model enables women to give birth safely at home by linking self-employed skilled midwives with public sector services. Sixty self-employed community midwives (CMs) from four districts were trained in essential obstetric and newborn care as well as FP, infection prevention, interpersonal communication, community involvement, basic business skills, and financial literacy. There has been an increase in the proportion of women assisted by a skilled attendant during birth, and CMs are providing injectables and contraceptive pills. This model is being scaled up across Kenya, with nearly 200 CMs in 13 districts having been trained.

Key Partners in Reproductive Health and Family Planning Research and Introduction

CONRAD

Family Health International

Georgetown Institute for Reproductive Health

Health and Family Welfare Centers (Bangladesh)

IntraHealth International

Jhpiego

Management Sciences for Health

Meridian Group International Inc

National Institutes of Health

Partner government ministries of health

PATH

Pathfinder International

Pfizer

Population Council

Save the Children

Schering AG

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

World Health Organization

HIV/AIDS

Areas of Research and Introduction: Five-Year Strategy 2006–2010	FY09 Funding \$77,377,000
Vaccines	\$28,477,000
Microbicides	\$45,000,000
Applied research and public health evaluation	\$3,900,000

Issues and Rationale

HIV infection rates continue to rise in many developing countries. An estimated 2.7 million new infections occur every year, and no cure is available. Infected persons worldwide number nearly 33 million, and in sub-Saharan Africa, almost 60 percent of infected individuals are women.

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 specific populations yield the best results. Current strategies for preventing HIV infection, including delay of sexual debut, partner reduction, and use of condoms, are often not possible for many women in developing countries. Novel technologies to prevent new HIV infections are needed to complement currently available methods of HIV protection. All existing and developing HIV/AIDS prevention approaches must be tailored to best serve specific at-risk populations.

Areas of Research and Introduction

Although widespread treatment programs are dramatically impacting the epidemic, they represent a lifelong commitment fraught with logistical burdens and reach only a fraction of those in need. Strategically expanded and sustainable treatment programs, in combination with new prevention technologies such as vaccines and microbicides, provide the best hope for controlling the expansion of the AIDS pandemic.

Since 2001, responding to congressional directives, USAID, through PEPFAR, has funded the International AIDS Vaccine Initiative (IAVI), a U.S.-based, nonprofit

organization that acts as a virtual pharmaceutical company to accelerate the development and clinical testing of HIV vaccine candidates. Inherent to this public-private partnership are collaborations among university, government, and private-sector groups to ensure that the appropriate resources are available for each phase of product development.

USAID support of microbicide research has led to the development of several potential products, two of which – Tenofovir 1% Vaginal Gel and Oral Truvada in Women – are in the final stages of international clinical trials to evaluate safety, effectiveness, and acceptability in preventing or decreasing HIV transmission. Other promising microbicide leads are advancing in the product development pipeline as a result of USAID funding for the International Partnership for Microbicides and other key players. USAID also supports targeted activities to ensure that after testing is completed, introduction and distribution of microbicides will be expedited in the developing country populations where the need is greatest⁵.

USAID supports applied research and public health evaluations to provide local implementing partners, donors, and national governments with the evidence base to improve HIV/AIDS services and inform policy. Specifically, projects are undertaken to facilitate: 1) improved solutions to HIV/AIDS service delivery issues, 2) improved utilization of applied research results, 3) improved capacity of developing country organizations to conduct applied HIV/AIDS research and use research results, and 4) new and improved HIV/AIDS program models available in developing countries.

Vaccine Development

Adding an effective AIDS vaccine to a comprehensive prevention strategy holds the most hope for diminishing the HIV pandemic. The search for this promising HIV prevention tool must be consistent despite the distinct challenge of developing and introducing such a product. Scientific advances in defining how the human immune

⁵ U.S. Agency for International Development. *Report to Congress: The USAID Strategic Plan for Microbicide Research and Development: Current Initiatives and Next-Generation Leads*. September 2009.

system attempts to protect itself against HIV are unfolding. The earliest events in natural infection, particularly in those who show an immune capacity to resist the virus, are beginning to inform new vaccine design; translating these events into a candidate vaccine holds great promise.

Through IAVI, USAID supports biomedical research in all phases of HIV vaccine clinical research and development (R&D) and other activities pivotal to the field. For IAVI's part, its R&D is focused on developing and evaluating novel vectors and vaccine designs and testing them in nonhuman and human trials while preparing communities so they can understand the wide variety of HIV vaccine trial results. IAVI supports two consortia made up of the most respected scientists in the field to inform immunogen design toward eliciting broadly neutralizing antibodies against HIV – key to the eventual success of an AIDS vaccine. They also support exceptional core immunology laboratory operations, which have driven regional quality standards and yielded new information about normal laboratory values for reference ranges.

In addition, USAID collaborates with the NIH, the U.S. Centers for Disease Control and Prevention (CDC), and the U.S. Military HIV Research Program (USMHRP) through the Partnership for AIDS Vaccine Evaluation. In 2008, IAVI, in conjunction with the CDC and USMHRP, released landmark work to provide data-defining normative laboratory values critical for designing and monitoring clinical trials among African populations. Laboratory tests of healthy African men and women on kidney and liver functions, as well as blood counts (e.g., hemoglobin, neutrophils and eosinophils), often fall outside established ranges. Researchers believe that these differences are largely environmental in nature due to ubiquitous encounters with common parasites and pathogens not typically found in the Western world.

Across Africa, drug and vaccine trial participants for diseases such as AIDS, TB, and malaria have been routinely disqualified from studies due to the standard use of laboratory reference ranges developed for Western populations. Now, due to the work of IAVI and its partners, reference ranges for healthy African trial volunteers have been established, creating appropriate criteria for the inclusion and exclusion of volunteers in testing for new, preventive health technologies, accurate health monitoring of patients throughout the course of a clinical trial, and, importantly, to guide treatment. These new data are critical in the design and monitoring of clinical trials, particularly trials of potentially lifesaving technologies among African populations.

In keeping with the mission of USAID, IAVI's work also builds local capacity at trial sites in human resources, laboratory, clinical, information technology, and other sustainable infrastructure. At the same time, it establishes reliable incidence and prevalence estimates through extensive cohort studies that define early HIV infection immunologic events and that guide decisions on where large-scale efficacy trials may be possible for vaccines and other new prevention technologies. USAID advisors ensure that IAVI establishes referral patterns to interface with existing U.S. Government programs for HIV/AIDS treatment, care, and prevention services under PEPFAR and the Global Fund to Fight AIDS, Tuberculosis and Malaria, while strengthening the capacity to accelerate clinical trials of AIDS vaccines in developing countries. These synergies set the stage for eventual product introduction and distribution. To inform public policy, USAID's partnership with IAVI supports analytical models to forecast estimates of global demand for AIDS vaccines.

Vaccines classically work by eliciting antibodies capable of disabling a virus from causing disease. Although it has proven difficult to stimulate a vaccine-induced protective antibody response against HIV, recent findings are providing promising insights into what forms of antibodies might be necessary for viral control. IAVI's continued efforts to identify naturally occurring antibodies capable of blocking a wide variety of HIV has recently yielded noteworthy findings from USAID-funded activities in developing countries where samples from otherwise healthy, HIV-positive volunteers have shown broadly neutralizing antibodies that are already providing very promising clues for vaccine development. Equally important is the production of functional and durable cellular responses able to thwart the transmitted virus. Among the serious challenges HIV poses to scientists trying to develop effective vaccines capable of counteracting the virus are its high rate of genetic variability, its capacity to escape natural immunity early after infecting its host, and its relentless ability to establish latent reservoirs of infection. IAVI's scientific agenda takes all these challenges into account.

IAVI's scientists are particularly focused on a few essential areas of viral behavior to inform and accelerate vaccine discovery. Important efforts include designing a vaccine that is ultimately capable of inducing antibodies that can be effective against many strains of HIV and optimizing lab techniques capable of more accurately and quickly measuring responses to HIV candidate vaccines, particularly in resource-poor areas.

As candidate vaccines are developed, they must be tested in humans – despite the challenges, potential risks, and

expense – while in parallel, plans are made for their eventual rollout. It is likely that first-generation HIV vaccines will be only partially protective, unable to completely prevent transmission and subsequent infection but effective enough to create immune responses that can mitigate the disease.

Epidemiological modeling exercises suggest that even a marginally effective vaccine would be powerful enough to result in stemming the flow of the pandemic. An AIDS vaccine could avert millions of infections in developing countries, and vigorous efforts to continue the biomedical search for this tool are imperative.

Lessons are being applied from new tools for other STI, TB, and malaria control efforts as they emerge. Plans are ongoing for the introduction of, and future access to, safe and effective HIV vaccines in developing-country settings, including engaging host country governments to register the new products, managing supply chain and logistics of vaccine delivery, developing acceptable protocols, and training health care workers to integrate this new technology into the dynamic landscape of HIV prevention.

U.S. Government-funded HIV vaccine R&D, in collaboration with the Government of Thailand, reported encouraging trial results on a vaccine that provided

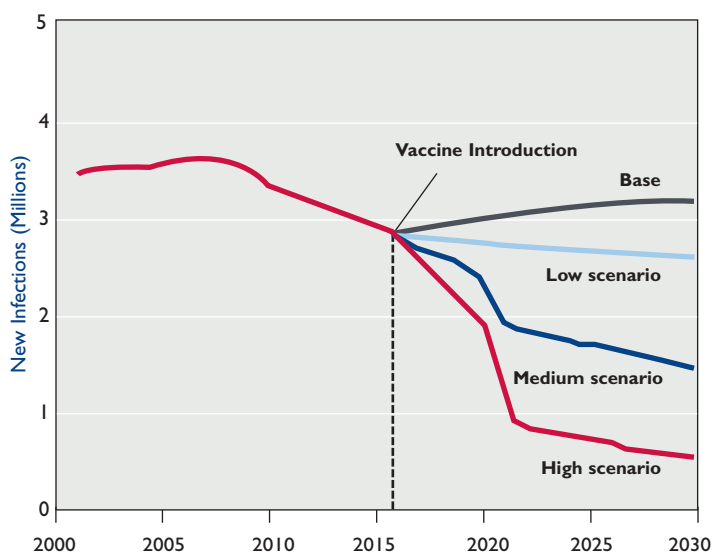
some protection against HIV infection. These new findings are a promising advancement in HIV vaccine research, which remains a relevant component of the comprehensive global AIDS response within a robust development agenda⁶.

Microbicides

Current strategies for preventing HIV infection are not available for many women in developing countries. Microbicides are a new class of health products that would provide women an effective barrier to sexually transmitted HIV. USAID’s strategy to promote the development of microbicides is to focus support on the advanced testing of the most promising candidates available. Clinical trials demonstrating the effectiveness of these products must be completed for approval by the appropriate regulatory agencies. Proof of concept (demonstration of effectiveness at reducing the risk of HIV acquisition) will speed up the availability of the best products, stimulate the future development of alternative or better products, permit the determination of the most appropriate preclinical models for evaluation of candidate products, and attract additional resources, investigators, and donors.

USAID’s role in microbicide development is coordinated through extensive representation and collaboration with the efforts of other U.S. Government agencies, as outlined in the 2006 HRRD.

Possible Scenarios for the Impact of an HIV Vaccine



Source: International AIDS Vaccine Initiative. “The Impact of an AIDS Vaccine in Developing Countries: A New Model and Preliminary Results.” Policy Research Working Paper #8. New York: IAVI. Available from <http://www.iavi.org> 2006.

In the history of pharmaceutical development, it has usually been necessary to evaluate a number of product leads to efficiently eliminate and prioritize candidates, even at the advanced stages of testing. Since early 2004, USAID has moved five promising candidates – Carraguard™, Ushercell™ (cellulose sulfate), and Savvy™ (C31G), Tenofovir 1% Vaginal Gel, and Oral Truvada in Women – into the final stages of clinical testing in international trials for their safety, effectiveness, and acceptability in reducing the risk of HIV transmission.

At the recommendation of the respective Data Safety Monitoring Boards, the Phase III trials for Savvy™ and Ushercell™ have been ended because completion at the sites chosen became futile, or because safety concerns became apparent only in the larger trial.

6 U.S. Agency for International Development. Forthcoming Report to Congress on a Coordinated Strategy to Accelerate Development of Vaccines for Infectious Diseases. Fall 2009.

Microbicides Research Strategy 2006–2010

Total FY09: \$45,000,000	
Strategy Themes	Areas of Research and Introduction: Five-Year Strategy
2006	<ul style="list-style-type: none"> → Continue Phase III large-scale clinical effectiveness trials initiated in FY 2004 and FY 2005 → 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	<ul style="list-style-type: none"> → Continue Phase III trials: Carraguard™, UsherCell™, and Savvy™ → Phase IIB/III trials: Tenofovir 1% 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	<ul style="list-style-type: none"> → UsherCell™ and Savvy™ trials ended by Data Safety Monitoring Board → Phase IIB/III trials: Tenofovir 1% Vaginal Gel and Oral Truvada in Women → Final results of Carraguard™ trial available → Continue to address policy and logistical issues for introduction → Continue to transfer manufacturing capacity
2009	<ul style="list-style-type: none"> → Phase IIB/III trials: Tenofovir 1% Vaginal Gel and Oral Truvada in Women → Continue to address policy and logistical issues for introduction → Continue to transfer manufacturing capacity
2010	<ul style="list-style-type: none"> → Phase IIB/III trials: Tenofovir 1% Vaginal Gel and Oral Truvada in Women → Continue to address policy and logistics for introduction: procurement and financing distribution networks within public and private sector, health delivery systems, information needs, licensing → Potential need for additional trials to be determined

The Carraguard™ Phase III trial was a milestone by being the first large clinical trial for effectiveness to be completed successfully. Although the product was found to be safe and acceptable, it did not significantly prevent infection in this trial. The Carraguard™ trial demonstrates for the microbicide field the feasibility and best practices of conducting large trials with extensive community involvement in developing countries. The findings of this trial are also important because Carraguard™ is also a key component of some next-generation microbicide formulations.

In FY09, USAID continues to support the large international and multiyear Phase IIB/III trials that are currently under way and evaluate the safety and effectiveness of Tenofovir 1% Vaginal Gel and Oral Truvada

in Women in thousands of volunteers (see Table 2). These trials will be completed in 2010 and 2012 and employ specific antiviral agents and unique delivery regimens, which may increase both user compliance and product effectiveness. These large clinical studies are required by the FDA, along with European and African regulatory agencies, to determine if these products can meaningfully reduce or prevent the sexual transmission of HIV. The initiation and progress of these landmark trials confirm the success of the USAID strategy in this research effort and are conducted in collaboration with other agencies and donors to the greatest extent possible to share costs and maximize the speed and efficiency of this work.

Other next-generation microbicide leads are in the product development pipeline and will also be tested clinically, if they continue to be promising in preclinical testing. Until one or more microbicides that are safe, effective, and acceptable are available for regulatory approval and introduction in developing countries, it is necessary to continue supporting research and development of the most promising leads. The present leads incorporate multiple agents that will prevent viral infection and inactivate the virus and/or prevent key replication steps. Careful targeting of funds to the essential early-stage research is required to allow these leads to advance to clinical testing. USAID's support for the International Partnership for Microbicides is particularly instrumental in advancing these early and very promis-

ing leads through preclinical development and into the early stages of clinical testing.

In the next year, as in the recent past, a large part of the USAID microbicide research and development budget will support the Phase IIB/III clinical studies for the most promising product leads. The remaining funds will be used to advance research on selected next-generation microbicide leads and develop capacity at sites for future clinical studies. This will entail targeted studies of local HIV incidence among risk groups and assessment and/or development of research capacity and community awareness in preparation for clinical trials of new microbicides. Some funds will also be used to prepare for the policy

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)
Population Council	7,150	7,227	6,505	7,137
CONRAD	14,097	13,982	13,506	15,560
Family Health International	13,776	12,551	14,914	16,683
WHO	100	406	837	700
Global Campaign for Microbicides	735	728	905	919
Int'l Partnership for Microbicides	2,347	2,500	3,269	1,000
CDC	623	1,405	2,715	1,120
PATH	286	676	1,004	1,075
AIM Project	186	125	351	253
Alliance for Microbicide Development	300	0	580	323
GH Tech	0	0	50	50
TOTAL	39,600	39,600	44,636	45,000

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

	Tenofovir 1% Vaginal Gel	Oral Truvada in Women
# of Sites and Locations	2 in South Africa	2 in Kenya 1 in Tanzania 2 in South Africa 2 in Malawi
Start of Screening and Enrollment	May 2007	July 2008
# of Volunteers to be Enrolled	980	3,900
Final Report Expected	Mid FY 2010	Early FY 2012
USAID Partner Conducting Trial	Family Health International, CONRAD, CAPRISA	Family Health International

and regulatory requirements that need to be addressed for the approval and introduction of these new products.

Applied Research and Public Health Evaluation

Through partnerships, USAID carries out HIV/AIDS program research and public health evaluations to improve coverage, quality, and effectiveness of HIV/AIDS programs in developing countries. The program also aims to strengthen local capacity in HIV/AIDS operations research and public health assessments through training and in-country collaborations. Major tasks aimed under this mechanism 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; and
- development and application of new technologies and intervention models in resource-poor settings.

Progress

Through FY09, a three-country effort aimed at developing and testing of multi-component program model for preventing HIV among vulnerable girls is in progress. A project for orphans and vulnerable children program research (OVC CARE – Comprehensive Action Research) is underway that aims to increase the evidence base for promising OVC program models. Another project on HIV prevention program research (Research to Prevention) was initiated to conduct operations research and program evaluations to address knowledge gaps in HIV prevention programming. A multi-country study under this project aims to evaluate program models addressing concurrent sexual partnerships. Other related activities include a synthesis of prevention program research from developing countries to clarify “what works,” and methodological research 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

CAPRISA

CONRAD

Constella Futures

Crucell

Department of Health and Human Services

Elizabeth Glaser Pediatric AIDS Foundation

Family Health International

GH Tech

Global Campaign for Microbicides

Global Fund to Fight AIDS, Tuberculosis and Malaria

Global HIV/AIDS Vaccine Enterprise

International AIDS Vaccine Initiative

International Clinical Epidemiology Network

International Partnership for Microbicides

Jhpiego

Johns Hopkins University

Macro International

MasiMax Resources, Inc./AIM Activity

Microbicide Research Working Group

National Institutes of Health Office of AIDS Research

Partner government ministries of health

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 2009 Funding: \$10,150,000
Vaccines	\$6,950,000
New drugs, formulations, and approaches	\$2,100,000
Delivery of proven interventions for malaria control	\$1,100,000

Issues and Rationale

Malaria remains one of the major causes of illness and death among children in Africa, and is estimated to account for 300 million to 500 million illnesses and nearly 1 million deaths each year, with 90 percent of those deaths in children under 5 years of age. More than 80 percent of these deaths occur in sub-Saharan Africa. Although eradication efforts during the 1950s and 1960s successfully eliminated or controlled malaria in other parts of the world, malaria has remained a major killer in sub-Saharan Africa due to a combination of natural and social conditions, including an ideal climate for malaria transmission, poverty, and political instability.

Approximately 3.2 billion people worldwide live in areas at risk of malaria transmission. Malaria places a tremendous burden on national health systems and individual families. Economists estimate 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. Although anyone living in an area where malaria is transmitted can be infected, three populations are particularly vulnerable: children under 5, pregnant women, and people with HIV/AIDS.

USAID, through the President's Malaria Initiative (PMI), is working to reduce malaria-related deaths through the expansion of coverage of four highly effective malaria prevention and treatment measures – insecticide-treated nets (ITNs), indoor residual spraying (IRS), treatment with artemisinin-based combination therapies and the expansion of intermittent preventive treatment for pregnant women. Initial data indicate a

possible decrease in the incidence and prevalence of malaria in focus countries. In spite of this progress, the intensification of an antimalarial drug and insecticide resistance underscores the urgent need for new technologies that can be used as part of malaria control efforts.

Areas of Research and Introduction

Vaccines

USAID's Malaria Vaccine Development Program (MVDP) has as its goal the development and introduction of vaccines into malaria control programs in developing countries. At the same time, the MVDP operates in the context of the worldwide malaria vaccine development effort. This includes the development of vaccines for travelers, including military personnel, as well as vaccines for residents of endemic areas, primarily children and pregnant women. This coordinated approach takes advantage of advances made by each program to help achieve the goals of all.

Progress

The GlaxoSmithKline Biologics (GSK) vaccine RTS,S/AS01b, currently the most advanced malaria vaccine (see the 2006, 2007 HRRD), has now begun pivotal testing to gather data for submission to regulatory bodies as a part of applications for licensure. A recent field trial on 5- to 17-month-old children in endemic areas of East Africa found a significant efficacy (50 percent) in those immunized with the vaccine compared to those immunized with a rabies vaccine. Over an approximately eight-month period, 8 percent versus 16 percent of the participants developed malaria respectively. If the applications for licensure are successful, it is expected that the vaccine will be available for introduction within the next four to five years. It remains to be seen whether these promising results will translate into a useful modality in malaria control programs.

Although the GSK vaccine is encouraging, it falls short of what is needed to achieve maximum impact on malaria morbidity and mortality. A 50 percent efficacy leaves one-half of children unprotected. Thus, as the GSK vaccine undergoes final pre-licensure evaluation, USAID MVDP remains focused on the development of more effective vaccines for control programs by filling

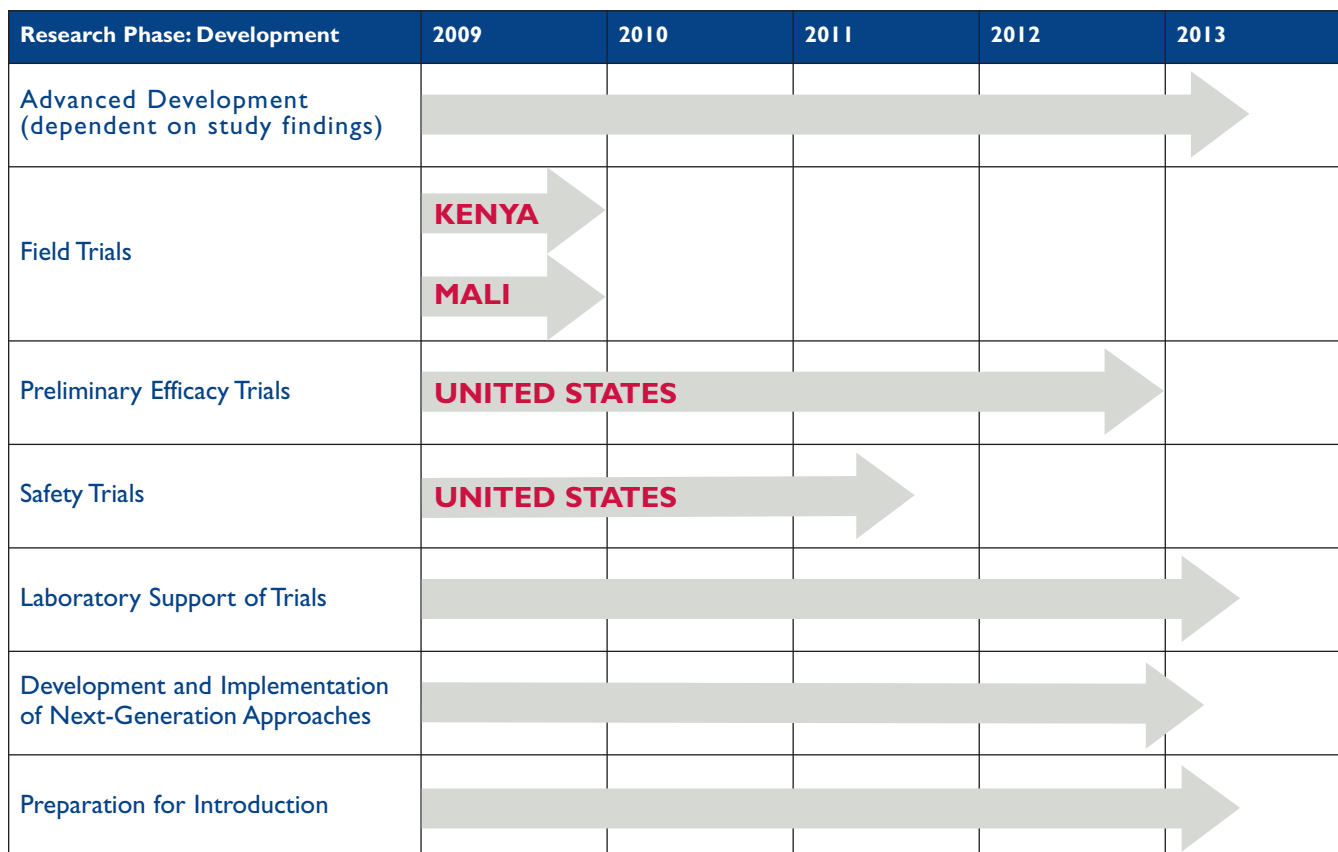
existing research gaps. Other development programs are focused on the GSK vaccine and on vaccine approaches designed for implementation in a future malaria eradication effort. Due to other priorities, the Bill & Melinda Gates Foundation, and thus the Malaria Vaccine Initiative at PATH (MVI), have recently deemphasized their efforts on the development of blood-stage vaccines. Based on the emphasis other funders have placed on vaccines targeting the parasite prior to its entry into the blood, and because of its potential to prevent illness, blood-stage vaccine development remains a major emphasis of the MVDP. In addition to continued attention to blood-stage vaccines, USAID MVDP, like MVI and the Military Malaria Vaccine Program, will increase its efforts to improve pre-blood-stage vaccines, building on the success of the GSK vaccine.

USAID collaborated with GSK and the Walter Reed Army Institute of Research (WRAIR) to conduct a follow-on safety and immunogenicity adult trial on the blood-stage vaccine FMP1/AS02A (found to be not efficacious, see HRRD 2008) in the United States

(complete) and in Kenya (ongoing). USAID, WRAIR, GSK, and the Kenya Medical Research Institute will use the results of this trial to determine if the level of safety and immunogenicity observed justifies more advanced evaluation for efficacy in a pediatric population. A separate pediatric efficacy trial examining the effects of a vaccine developed through USAID support was conducted in collaboration with Walter Reed Army Institute of Research, GSK, the National Institute of Allergy and Infectious Diseases, the University of Maryland Center for Vaccine Development, and the Bandiagara Malaria Project of the Malaria Research and Training Center, University of Bamako, Mali. Planned unblinding of the study in late FY08 has been delayed, and the results of the trial remain pending. The two aforementioned trials are on blood-stage vaccines, albeit targeting different molecules in the parasite.

MVDP, with the Naval Medical Research Center, has completed a trial of a malaria vaccine presented as a recombinant adenovirus; i.e., a virus that contains malaria genes. Unfortunately, the vaccine showed no

Figure 1. USAID Malaria Vaccine Development Program Activities



efficacy. A further trial is being conducted in which the relevant genes are being presented in the form of DNA (the “priming”) and the subjects are later “boosted” with the adenovirus vector vaccine. This regimen is believed to offer a greater chance of success. With MVI, USAID is supporting a major program to evaluate a second type of prime-boost regimen using two types of adenoviruses. The MVDP also supports a program of preclinical research and development to feed the pipeline of new investigational vaccines.

It is the history of vaccine development that most investigational vaccines fail to pass all the requirements for licensure and introduction. MVDP continues to focus on the development of alternative vaccines that could work through different mechanisms to broaden the base of the malaria vaccine development enterprise, and maintain a robust pipeline of alternative products should early vaccines not be successful. To further this strategy, USAID will continue to work closely with partners, both those funded by USAID – MVI, U.S. Department of Defense, and, since 2007, NIAID – as well as those with whom USAID coordinates activities without provision of funding.

Figure 1 outlines USAID’s current and planned malaria vaccine development activities, assuming continued support for efforts in further development of vaccines shown to be efficacious.

New Drugs, Formulations, and Approaches

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 will target pregnant women and children under 5, the two most vulnerable groups
- (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

Progress

Since 2004, USAID has provided \$1.5 million per year to the Medicines for Malaria Venture (MMV), a non-profit, public-private partnership created to replenish and then sustain the global pipeline of antimalarial drugs. MMV’s goal is to register at least one new antimalarial drug every five years, with an emphasis on

drugs that are effective against drug-resistant strains of *Plasmodium falciparum* and can be used safely in young children and pregnant women. The research and development activities 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 38 different pharmaceuticals at various stages of development, from drug discovery to Phase III human field testing and registration. Several of these products are of particular interest to USAID:

- A dispersible pediatric formulation of lumefantrine-artemether (Coartem®), which was registered with SwissMedic in December 2008 and is already being delivered to malaria-affected countries.
- Dihydroartemisinin-piperaquine and pyronaridine-artesunate, two new and novel ACTs, which should have their dossiers submitted to regulatory authorities in Europe in 2009, with approval expected in late 2009 or early 2010.

To complement this funding, USAID also supports the UNICEF/United Nations Development Program (UNDP)/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, which has focused on operational and field research related to ACTs. These activities include:

- A registry in countries using ACTs to assess the safety of ACTs in pregnant women;
- Evaluations of the use of ACTs by community health workers with and without rapid diagnostic tests; and
- Evaluations of the integrated management of malaria and acute respiratory illnesses at the community level.

Delivery of Proven Interventions for Malaria Control

USAID, through PMI, is supporting activities to enhance the delivery of evidence-based malaria control interventions in sub-Saharan Africa. Proven tools for the primary prevention of malaria are ITNs and IRS. ITNs provide a physical barrier in combination with an insecticide that can kill or repel mosquitoes. To date, only one class of insecticides, the synthetic pyrethroids, is practical for wide-scale use on netting material, increasing the probability of the development and spread of drug resistance.

There are 12 different WHO-approved insecticides for IRS, including DDT, enabling programs to rotate insecticides in an effort to combat the development and spread of insecticide resistance. Correctly applied, IRS can be effective for periods of 6 to 12 months, depending on a variety of factors, such as the seasonality of malaria transmission, the class of insecticide, and the initial concentration used.

Long-lasting insecticide-treated nets (LLINs), which can maintain their insecticidal properties for up to 20 washings, can be delivered through a variety of public health strategies. Countries are now rapidly expanding delivery of LLINs through large-scale campaigns, especially in high-transmission zones. In addition, a renewed emphasis on IRS in sub-Saharan Africa has led to an expansion of spray programs beyond high-transmission and epidemic-prone districts to areas with stable malaria transmission.

Given the increased likelihood of these efforts, USAID is supporting research in sub-Saharan Africa to examine the potential impacts of the introduction of LLINs in communities that use IRS and the epidemiological and entomological impacts of the LLIN/IRS combination.

Key Partners in Malaria Research and Introduction

Bandiagara Malaria Project of the Malaria Research and Training Center, University of Bamako, Mali

GenVec, Inc.

GlaxoSmithKline, PLC

Johns Hopkins University

Kenya Medical Research Institute

Malaria Research and Training Center

Medicine for Malaria Venture

National Institute of Allergy and Infectious Diseases

Partner government ministries of health

PATH's Malaria Vaccine Initiative

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

Tuberculosis

Issues and Rationale

An estimated one-third of the global population – 2 billion people – is infected with tuberculosis (TB). TB kills more than 1.7 million people per year and is economically devastating to families and communities worldwide. TB disproportionately affects poor countries and marginalized populations, with developing countries accounting for 95 percent of all TB cases and 98 percent of all TB deaths.

Areas of Research and Introduction

USAID invests in research that will improve the performance and public health impact of 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, 3) preventing disease, and 4) increasing access to directly observed treatment, short course (DOTS).

Tremendous momentum is building toward the development of new tools to fight TB. New diagnostics are being tested in the field and adopted into global policy, new drugs that may be effective for drug-sensitive and drug-resistant disease have progressed into Phase III trials, and new vaccines may be ready for Phase III trials by 2011. USAID has fully aligned its TB funding with the 2006 strategy presented to Congress, and as such, has been a leading supporter of late-stage research that is having a direct effect on country-level TB programs. Between FY07 and FY08, USAID's investments in research related to TB increased by 18 percent. USAID has remained an active partner in the Stop TB Partnership's Working Groups for new diagnostics, new drugs, and new vaccines. USAID staff also chairs the Retooling Task Force, which aims to accelerate uptake of new technologies in disease-endemic countries.

In 2008, USAID awarded a competitively bid cooperative agreement for a comprehensive research program. This project consolidates USAID's research efforts to fill gaps in evidence at a global level and provides USAID Missions with access to a consortium of research experts able to assist in the design and implementation of locally relevant research. Through this cooperative agreement,

USAID will support research to optimize the effectiveness of existing technologies and approaches while supporting late-stage clinical trials, field evaluations, and operational research to bring new tools and approaches to the fore. It will also ramp up efforts to prepare the field for the introduction of new technologies, testing novel techniques to deliver these tools/approaches at country level, and address barriers to access services. USAID will capitalize on this new project to continue to move successes from research into policy and practice.

USAID is drawing on its unique positions – namely its field presence and prominent roles in the Stop TB Partnership – to promote research that is relevant to the high-burden countries and ensure that important research results are brought into global policy.

New Drugs/Improved Regimens

Last year, approximately 36 percent of USAID's research funding for TB was used to support the evaluation of promising new drugs. The Agency also added a fourth drug to its portfolio. All of the drugs supported by USAID are in late-stage clinical trials (i.e., at least Phase IIB), promising to shorten drug regimens and/or add other compounds to the arsenal available to fight drug-resistant disease in the near future.

USAID is leading several key clinical trials that may impact current treatment standards. One recently completed trial compared the treatment outcomes of patients given fixed-dose combination tablets versus loose formulations. This trial confirmed that the current standard of fixed-dose combination drugs is not contributing to the emergence of drug resistance. However, there are some operational issues related to fixed-dose combinations that will need to be taken into account through our implementation programs. Through the CDC, USAID is supporting an evaluation of treatment for drug-resistant TB. The study completed enrollment in the past year. In addition, an ongoing study of the potential drug interactions between anti-TB drugs and antiretrovirals for HIV/AIDS made considerable progress in the last year, and a preliminary analysis of the results is currently being undertaken.

Tuberculosis Research Strategy 2006–2010

Total FY09 Funding: \$9,400,000	
Strategy Themes	Areas of Research and Introduction: Five-Year Strategic Plan
New Drugs Improved Regimens	Identify and introduce new, shorter treatment regimens, new second-line drugs for resistant disease, and drugs compatible with antiretrovirals (ARVs) for HIV; support trials of drugs at Phase IIB and beyond
	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; support trials of diagnostics at Phase IIB and beyond
New Vaccines*	Test a vaccine that prevents infection with TB; support trials of vaccines at Phase III and beyond
	Develop an effective vaccine to protect TB-infected individuals from developing TB disease; support 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 ARVs for children and adults
	Test approaches to increase HIV testing among TB patients as an entry point to care
Improve the Performance of and Accessibility to DOTS Programs	Determine effective initiation, duration, and programmatic impact of preventive therapy regimens in consideration of ARV use
	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.

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

New Diagnostics

USAID has supported research related to alternative approaches to collecting and preparing sputum smears for detecting TB. In addition, evaluations of the effectiveness of LED fluorescent microscopy in field conditions were completed in 2008. The results from these lines of research were consolidated in the past year and will be presented in late 2009 to a WHO expert committee for proposed changes to international policy. USAID continues to fund research investigating alternative diagnostic algorithms and approaches, as well as

developing new technologies to screen and test for TB. In particular, USAID support is targeting the optimization of smear microscopy for routine cases, rapid detection of drug-resistant disease, and improvements in TB diagnosis among people infected with HIV/AIDS.

New Vaccines

USAID continues to work closely with NIH and the vaccine community to monitor the progress of vaccine research. As presented in the 2006 HRRD Report to

Congress, NIH will support vaccine research through the development phase and will look to USAID to support field trials of vaccines that have progressed to Phase III and would have an important public health impact. It is expected that this support may occur as soon as 2011.

Improved Performance of and Accessibility to DOTS Programs

Through the USAID Missions, important operational research has been conducted to better inform programmatic investments and improve the performance of national TB programs. This year, for example, the Missions supported research to assess interventions to overcome barriers to coordinated TB-HIV care and poor treatment compliance among patients.

Key Partners in Tuberculosis Research and Introduction

Aeras

Foundation for Innovative New Diagnostics

Global Alliance for TB Drug Development

International Union Against TB and Lung Disease

Johns Hopkins University

Partner government ministries of health

PATH

Stop TB Partnership Working Groups

University of Alabama

U.S. Centers for Disease Control and Prevention

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

WHO Special Programme
for Research and Training in Tropical Diseases

World Health Organization

Health Systems Strengthening

Issues and Rationale

Health systems strengthening is a long-term, multi-faceted area of USAID programming and one that is critical to sustained improvements in health outcomes in developing countries. 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 challenges and gaps⁷. The challenges to high-quality, accessible, and affordable health services are described below:

- The vast majority of service delivery in developing countries does not benefit from modern quality improvement approaches, even though these approaches have proved to be highly effective in even the poorest health systems. These systems are burdened

⁷ U.S. Agency for International Development. Health Systems Report to Congress. October 2009.

Health Systems Strengthening Research Strategy 2006–2010

Total FY09: \$11,645,701	
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
Medical Supplies, Vaccines, and Technology	Improve knowledge of the presence of sub-standard and counterfeit products on the market
	Explore their role in the emergence of drug resistance
	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

by service delivery that does not follow evidence-based standards and by inefficient practices. These problems are not addressed by training alone.

- Although the health workforce represents about 70 percent of the cost of health care, management of human resources in developing countries is widely acknowledged to be weak. The general principles for maximizing the productivity of the workforce are well established, but these principles need to be adapted to each health system, and many obstacles to change exist in this politically sensitive area. Producing more health workers is an important strategy in many countries, but every developing country also needs to make better use of the human resources that it has.
- Few developing countries have sufficiently strong and effective health information systems to permit adequate monitoring of progress toward their health goals, including the identification of problems and needs, in order to make evidence-based decisions on health policy and allocate scarce resources optimally.
- An estimated 30 percent of the world's population lacks regular access to medicines, with this figure rising to more than 50 percent in the poorest areas of Africa and Asia. Health programs are further challenged by the need to ensure that medicines are of assured quality and safety, and are used appropriately by providers and consumers. Health systems with inadequate regulatory capacity are ill-equipped to control the entry of counterfeit medicines (representing as much as 10 percent of sales in some developing countries) and substandard products into the marketplace. Along with inappropriate medicines use, access to poor quality medicines can contribute to the more rapid emergence of resistance and the need to use more costly second-line medicines, with potentially longer duration of treatment for patients.
- An estimated 180 million people in developing countries suffer from financial catastrophe because of the cost of health care. The root causes of this are high out-of-pocket expenditures and scant availability of financial subsidies in most low-income countries. According to Transparency International, 40 percent of the most corrupt nations in the world are also the poorest countries in the world. The lack of accountability and transparency in governance leads to poorly managed and underfunded health systems, which in turn results in low availability of basic, lifesaving health care.

Areas of Research and Introduction

USAID conducts health systems research and evaluations to identify, test, and facilitate host country introduction and scale up of best practices that reduce the burden of disease due to the major causes of mortality and severe morbidity. USAID's health systems research meets four criteria: a) it is relevant to the successful implementation of health interventions in HIV/AIDS, malaria, tuberculosis, reproductive health and family planning, maternal and newborn health, and nutrition; b) it has the potential to improve access, quality, and/or affordability; c) it can achieve demonstrable and measurable improvement within three to five years; and d) it is suitable for sustained use in low-resource settings.

Using Improvement Collaboratives to Strengthen Service Delivery

USAID expands the use of modern quality improvement approaches that are widely used in the U.S. health system in developing countries. With some adaptation, these approaches have produced promising improvements in health care in a range of countries and across a number of health services. The most promising of these approaches is the improvement collaborative approach, pioneered by the Institute for Healthcare Improvement in Boston, which organizes teams of providers in a number of facilities to work together to improve the organization of a specific service. Using their own insights, the teams test changes in the way they deliver services and share what they learn with all the other teams.

The Bolivia tuberculosis collaborative, aimed at strengthening the National TB Control Program's performance, addressed four main TB control problem areas: a) increasing detection of respiratory suspects and TB new cases, b) increasing practice of DOTS, c) increasing cure rates and treatment success rates, and d) reducing abandonment rates. After developing a tested package of program improvements, teams of providers participated in an organized effort to spread improved practices, reaching 217 additional facilities. These facilities achieved important improvements in TB cure rates, treatment success rates, case detection, and treatment abandonment.

One of the oldest collaboratives is in Niger, where improved practices in obstetrical care, covering 32 percent of the country's maternities, reduced postpartum hemorrhage to less than 10 percent of baseline levels. These improvements have been sustained for more than three years, benefiting more than 100,000 deliveries. These teams have gone on to improve the care of the newborn, as compared to evidence-based quality standards (Figure 1).

Figure 1: Niger: Improving Essential Newborn Care and Practice of Immediate Breastfeeding in EONC Collaborative Site, January 2006–September 2008

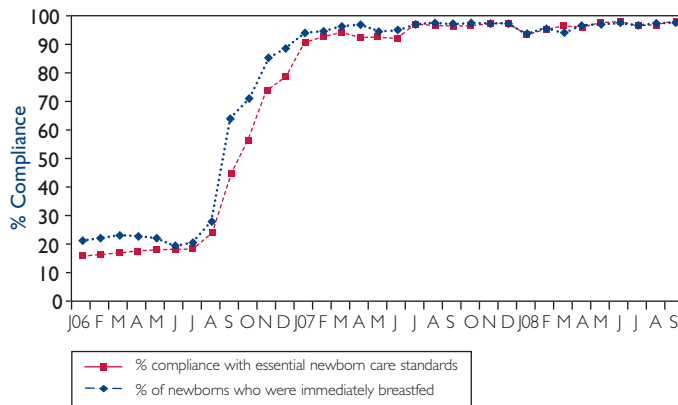
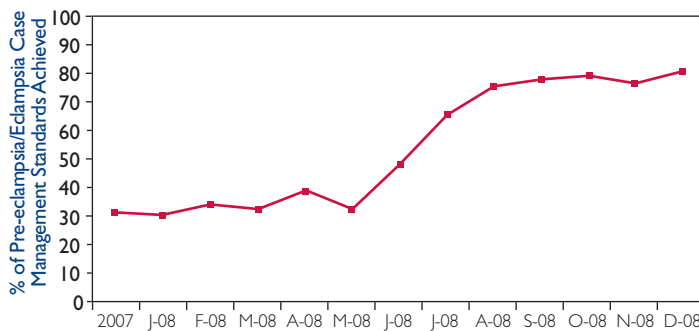


Figure 2: Niger: Improving Quality of Case Management for Pre-eclampsia/Eclampsia, 31 MOH Facilities, 2007 (Baseline) and January–December 2008



These teams also introduced pre-eclampsia and eclampsia improvements in 32 facilities as part of a second phase (Figure 2).

Gauging and Improving Health Workforce Satisfaction and Productivity

USAID’s health workforce research aims to improve tools to measure workforce satisfaction and productivity. A follow-up study on workforce retention in Uganda showed that, contrary to popular perception, average annual attrition rates are low (1.2 percent) in the public sector, but much higher (13 percent) in the private, not-for-profit sector. Major causes are leaving assigned posts and retirement. Rates varied among different categories of health workers, indicating the need for different moti-

vation mechanisms for each, which are now being identified. Based on this experience, USAID is refining tools for measuring retention and sharing the Uganda case study for use in other countries.

Additional workforce productivity studies were conducted by USAID in Zanzibar and by the National Institute for Medical Research in mainland Tanzania to determine productivity levels and correlates of increased productivity as a basis for global guidance. An emphasis was placed on implementation at the facility level. Applying findings from these workforce productivity studies, the MOH worked with facility stakeholders to select and implement interventions that are feasible, evidence-based, and inexpensive. Early assessment indicated increased job satisfaction and worker intentions to remain in these positions.

From this work, USAID is continuing development of a productivity improvement model, including a package of measures and tools, to improve productivity at what are traditionally less-productive times for use in other countries.

Gender-based inequality and violence in the workplace negatively impact the individual worker and her/his ability to perform effectively. The frequency with which this occurs is often not recognized or acted upon due to its socially sensitive nature. To address this, the ministries of labor, health and gender and the Health Workers Union in Rwanda, with support from USAID, are using findings from a health facility worker survey to create policies and programs to protect workers from interpersonal violence and gender discrimination. The study found that female health workers face negative stereotypes and discrimination in hiring and promotion due to pregnancy and family responsibilities, and that a culture of respect and gender equality at work lowers the risk of violence. Study results are being used to advocate for ratification of international labor codes related to maternity protection and workers with family responsibilities. The work in Rwanda is serving as a model for efforts in other countries.

As part of the global initiative to reduce maternal and child (MCH) mortality, USAID is supporting the expansion of the number of community health workers contributing to effective MCH services. To enable monitoring of the success of the initiative in terms of the number of functional CHWs, USAID supported the development of a new tool to systematically rate programs and provide rapid, consensus-based measurements that can be applied periodically to track overall progress. In 2009, field tests were conducted in Nepal to validate

this tool. Once finalized, the tool, along with its associated guidelines and the results of its application, may be used to monitor and strengthen MCH programs worldwide. Since this tool may be easily adapted to other types of health services, it should also prove useful for HIV/AIDS, tuberculosis, and other USAID priorities.

Introducing New Methods for Information Management

The Monitoring & Evaluation (M&E) System Strengthening Tool was developed collaboratively by USAID, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Office of the U.S. Global AIDS Coordinator, UNAIDS, WHO, the World Bank, the Health Metrics Network, and Roll Back Malaria to allow stakeholders to evaluate how the various donor-supported M&E activities are linked and integrated within the national M&E system, and to develop costed action plans to strengthen this system. The Global Fund mandates use of this tool as part of its grant negotiation process and has applied it in 70 countries for HIV/AIDS activities, in 53 countries for malaria activities, and in 57 countries for TB activities.

To provide the highest-quality data to inform global HIV/AIDS efforts, USAID's Demographic and Health Surveys (DHS) and AIDS Indicator Surveys (AIS) are important sources for global efforts coordinated by UNAIDS to estimate HIV/AIDS prevalence among the general population. USAID partners have also created statistical models to estimate the HIV prevalence rates of non-household populations, such as inmates, the homeless, and sex workers.

Understanding and Protecting the Effectiveness of Medical Products

Understanding the community and facility factors that influence antimicrobial resistance (AMR) is critical to the design and implementation of appropriate interventions. USAID supported the development of an AMR module for population-based surveys, which uses the same structure as the other modules of the DHS and is accessible for country-level use through the DHS Web site. USAID also supported comprehensive baseline surveys to identify facility-related issues and factors that impact AMR (Ethiopia) and assess Accredited Drug Dispensing Outlet dispensers' knowledge, practices, and attitudes relating to AMR and antibiotic use (Tanzania). Information obtained from these surveys is being used to

design evidence-based and locally appropriate AMR advocacy and containment interventions.

The availability of case and drug management information is critical to the success of TB programs. An electronic tool that tracks patient and drug management information, developed with USAID support, has been adopted for nationwide implementation in Brazil, and is now being implemented in the Philippines, Dominican Republic, and Ukraine. In Brazil, the tool has resulted in an increased rate of case detection among contacts and improved availability of needed medicines.

A country's list of essential medicines should satisfy the priority health care needs of the population. In Namibia, USAID assisted the MOH to develop and implement technical guidelines for evaluating new medicines. As a result, the essential medicines list (EML) was updated to include important medicines related to antiretroviral therapy (ART) using the most cost-effective products. The process and guidelines for evaluating new medicines have made the EML selection process transparent and increased confidence in the system by health care workers.

USAID, in collaboration with WHO, supported a multi-country study on the quality of antimalarials in sub-Saharan Africa. The study results will provide representative information about the proportion of sub-standard and counterfeit antimalarials in Africa and will provide an evidence base to guide strategies and implementation plans for the provision of quality antimalarials to result in evidence-based strategies and implementation plans to improve medicines quality.

USAID also established, or strengthened, post-marketing surveillance systems to sample and test the quality of medicines in Latin America, Africa, and Southeast Asia. USAID supported the sampling of approximately 900 antimalarials, TB and HIV/AIDS medicines, and antibiotics this year in Bolivia, Brazil, Guyana, Suriname, Paraguay, Peru, Vietnam, Laos, Cambodia, Philippines, Senegal, and Madagascar. The post-marketing surveillance data gathered in Southeast Asia were instrumental in the success of a regional anti-counterfeit operation that led to the withdrawal of \$6.7 million worth of spurious medicines. Overall, these results have helped raise local stakeholder awareness on the need to improve the quality of medicines in the market. In the Latin American countries, it has also led to the initiation of regulatory system improvements, including strengthening registration and national quality control laboratory capacity.

Improving Evidence and Practice in Health Financing

Improvements in health financing in developing countries depend on better understanding of current financing practices and on better evidence about large-scale approaches that work. USAID, in collaboration with the Health Research Unit of the Ghana Health Service, analyzed the impact of Ghana's National Health Insurance (NHI), which covered 6 percent of the population by the end of 2008. Implementation of the insurance scheme led to significant improvements in health care utilization for illness or injury and reductions of out-of-pocket expenditures for care, including expenditures for hospitalization. The findings from this study, as well as the operational challenges associated with scaling up the NHI, will be essential in informing other countries considering social health insurance.

The National Health Accounts (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. Together with these partners, USAID has developed methodologies for NHA subaccounts to measure total national spending for specific health issues. More than 50 estimations have been carried out in more than 25 countries to date, including subaccounts for HIV/AIDS, malaria, tuberculosis, reproductive health, and child health. Policymakers have successfully used data collected by NHA subaccounts to inform on health policy, mobilize resources, monitor programs, and increase transparency and accountability.

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 (HAPSAT) and the SPECTRUM suite of models support priority setting and resource allocation decisions by partner governments planning a national response to HIV/AIDS. These models use detailed epidemiological, demographic, and economic data to estimate the financial and human resources required to sustain and/or scale up a portfolio of HIV/AIDS programs and facilitate broad-based policy dialogue in the formulation of sustainable national strategies. HAPSAT has been piloted in Zambia and implemented in Cote d'Ivoire, Nigeria, Tanzania, and Ethiopia, with future introductions of this tool planned in Haiti and Vietnam. SPECTRUM has been used to facilitate program dialogue in Rwanda, South Africa, Namibia, Uganda, Botswana, and Nigeria. It is also used to support

Key Partners in Health Systems Strengthening Research and Introduction

Abt Associates
Academy for Educational Development
Alliance for Health Systems Research
Alliance Group (Malawi)
Bill & Melinda Gates Foundation
Danida
Ghana Health Research Unit of Ghana Health Service
Global Alliance for Vaccines and Immunizations
Global Drug Facility
Global Health Workforce Alliance
Green Light Committee
Health Metrics Network
IntraHealth International
Irish Aid
Macro International
Management Sciences for Health
Miz-Hasab (Ethiopia)
Open Society Institute
Partner government ministries of health
Rwanda National Malaria Control Program
Stop TB Task Force
Swedish International Development Agency
The Global Fund to Fight AIDS, Tuberculosis and Malaria
The Partnership for Child Health Care, Inc./BASICS
U.K. Department for International Development
UNAIDS
UNFPA
University Research Corporation
U.S. Centers for Disease Control and Prevention
U.S. Pharmacopeia Drug Quality and Information
U.S. President's Emergency Plan for AIDS Relief

UNAIDS' bi-annual global projections of HIV/AIDS impact and resource needs, and is currently being used to assess the implications of proposed WHO revisions to its HIV/AIDS treatment guidelines. Both models are routinely updated as new knowledge becomes available.

Assessing and Improving Health Governance

Strong leadership and governance contribute to reducing health sector corruption and increasing accountability. USAID is advancing research to understand the effects of disease-focused health initiatives on country health systems, beginning with a comparative analysis of data from the System-Wide Effects of the Global Fund (SWEF) assessments conducted in Benin, Ethiopia, and Malawi. SWEF studies in Ethiopia indicated that with the rapid launch of new services, more remains to be understood about the impact of the Global Fund on the country's health system. The multi-donor Global HIV/AIDS Initiatives Network, which continues these studies of health systems, grew out of the early SWEF work.

USAID is collaborating with international agencies to improve the evidence on benchmarking health system

performance. A Web-based database that consolidates key demographic, health status, economic, and governance indicators was launched in 2008. This health systems database compiles and analyzes country data from multiple sources, provides charting options, and generates automated country fact sheets, helping users to obtain a rapid overview of a country's health system performance in comparison to both its geographic and income group peers.

Improved governance contributes to increased utilization of priority health services. In collaboration with the Health Systems Action Network, USAID supported a survey on the practice of good governance in the health sector. The results of this survey were used to develop resource papers on governance concepts, issues, and programming options. USAID also developed guidance for how to subcontract with NGOs in fragile states in ways that promote longer-term health systems strengthening.

Addendum I: Core Funding for Targeted Health Issue Strategies¹

Health Issue	Product	FY 2006 Obligated Funds	FY 2007 Obligated Funds	FY 2008 Obligated Funds	FY2009 Funding
Maternal and Newborn Health	Healthy Pregnancy and Birth Care Outcomes	\$1,283,000	\$1,634,000	\$1,634,000	\$865,000
	Maternal Mortality Measurement Tools	\$130,000	\$122,000	\$122,000	\$0
	New Pregnancy and Birth Interventions and Introduction	\$4,065,000	\$2,700,000	\$2,700,000	\$3,805,236
	Neonatal Research and Newborn Care Practices	\$1,600,000	\$2,552,000	\$2,552,000	\$3,775,650
	Total	\$7,078,000	\$7,008,000	\$7,008,000	\$8,445,886
Child, Environmental, and Urban Health	Community-based Pneumonia Treatment	\$650,000	\$638,000	\$638,000	\$1,204,350
	Diarhea Management: Reversing Declining Rates of Use of ORT ²	\$755,000	\$270,000	\$120,000	\$160,000
	Reducing Exposure to Indoor Air Pollution	\$70,000	\$0	\$0	\$300,000
	Water Supply, Sanitation, and Hygiene	\$0	\$0	\$0	\$400,000
	Urban Health	\$0	\$0	\$0	\$100,000
Total	\$1,475,000	\$638,000	\$758,000	\$2,164,350	
Nutrition	Vitamin A Deficiency Prevention and Control ³	\$759,000	\$350,000	\$350,000	\$400,000
	Iron–Anemia Prevention/Rx Packages	\$376,600	\$380,810	\$380,810	\$580,810
	CMAM (Formerly Community Therapeutic Care)	\$1,100,000	\$1,200,000	\$1,200,000	\$1,000,000
	Dietary Quality and Diversity	\$0	\$150,000	\$600,000	\$700,000
	Antenatal Multiple Micronutrient Supplementation	\$180,000	\$0	\$0	\$0
Total	\$2,415,600	\$2,080,810	\$2,530,810	\$2,680,810	
Reproductive Health and Family Planning	Contraceptive Technologies	\$10,500,000	\$13,630,000	\$10,223,000	\$13,071,000
	Improved Use and Services Delivery	\$14,000,000	\$15,660,000	\$19,450,000	\$17,126,000
Total	\$24,500,000	\$29,290,000	\$29,673,000	\$30,197,000	
HIV/AIDS	Vaccines	\$28,710,000	\$28,710,000	\$28,477,000	\$28,477,000
	Microbicides	\$39,600,000	\$39,600,000	\$44,636,500	\$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
	Total	\$70,060,000	\$71,560,000	\$77,013,500	\$77,377,000
Malaria	Vaccines	\$6,200,000	\$7,000,000	\$7,000,000	\$6,950,000
	New Drugs, Formulations, and Approaches	\$3,200,000	\$3,000,000	\$3,000,000	\$2,100,000
	Delivery of Proven Interventions for Malaria Control	\$0	\$0	\$0	\$1,100,000
Total	\$9,400,000	\$10,000,000	\$10,000,000	\$10,150,000	
Tuberculosis	New Drugs	\$2,400,000	\$3,000,000	\$3,000,000	\$3,000,000
	Improving Performance of and Access to DOTS ⁴	\$2,790,000	\$4,662,090	\$4,500,000	\$6,400,000
Total	\$5,190,000	\$7,662,090	\$7,500,000	\$9,400,000	
Health Systems Strengthening ⁵	Service Delivery (Approaches and Technologies)	\$862,100	\$2,202,200	\$1,005,280	\$1,190,000
	Human Resources for Health	\$896,900	\$578,100	\$622,950	\$1,300,000
	Information	\$4,176,981	\$3,696,524	\$4,200,000	\$6,107,000
	Medical Supplies, Vaccines, and Technology	\$614,389	\$564,187	\$715,000	\$705,000
	Financing	\$555,000	\$912,000	\$345,000	\$1,688,701
	Leadership and Governance	\$400,000	\$410,000	\$445,000	\$655,000
Total	\$7,505,370	\$8,363,011	\$7,333,230	\$11,645,701	
TOTAL Funding		\$127,623,970	\$136,601,911	\$141,816,540	\$152,060,740

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

^{2,3} As described in the 2006 HRRD, research findings are currently being introduced into programs.

⁴ Re-classification of the category of research based on the new OP documentation process.

⁵ The projected FY 2006 funding figures previously published in the 2006 HRRD did not capture all health systems research activities. USAID uses WHO'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 HRRD and uses a more comprehensive list of products in order to capture progress in this area of work more completely.

Addendum 2: Key USAID Global Health Research and Introduction Partners

Abt Associates
Academy for Educational Development
Aeras
Aga Khan Foundation
Aga Khan University
Alliance for Microbicide Development
Becton, Dickinson and Company
Bill & Melinda Gates Foundation
Boston University
Canadian International Development Agency
Catholic Relief Services
Christian Reformed World Relief Committee
Concern Worldwide
CONRAD
Constella Futures
CORE Group
Crucell
Danida
Elizabeth Glaser Pediatric AIDS Foundation
European Commission
Family Health International
Foundation for Innovative New Diagnostics
GenVec, Inc.
Georgetown Institute for Reproductive Health
GlaxoSmithKline, PLC
Global Alliance for Improved Nutrition
Global Campaign for Microbicides
Global HIV/AIDS Vaccine Enterprise
Helen Keller International
ICDDR,B (Bangladesh)
International Aid
International AIDS Vaccine Initiative
International Clinical Epidemiology Network
International Confederation of Midwives
International Federation of Obstetricians and Gynecologists
International Food Policy Research Institute
International Partnership for Microbicides
International Research Committee
IntraHealth International
Jhpiego
Johns Hopkins University
Kenya Medical Research Institute
Macro International
Malaria Research and Training Center
Management Sciences for Health
MasiMax Resources, Inc./AIM Activity
Medicine for Malaria Venture
Microbicide Research Working Group
Micronutrient Initiative
National Institute of Allergy and Infectious Diseases
National Institute of Child Health and Human Development
National Institutes of Health, Office of AIDS Research
ORC/Macro
PATH
PATH's Malaria Vaccine Initiative
Population Council
Population Services International
Save the Children
Schering-Plough
Stop TB Partnership Working Groups
Synergy Project
The Futures Group
The Global Fund to Fight AIDS, Tuberculosis and Malaria
The Partnership for Child Health Care, Inc./BASICS
U.K. Department for International Development
UNICEF
University of Aberdeen (Scotland)
University of Alabama
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 Corporation
U.S. Centers for Disease Control and Prevention
U.S. Department of Health and Human Services
U.S. Food and Drug Administration
U.S. Military HIV Research Program
U.S. Naval Medical Research Center
U.S. Pharmacopeia Drug Quality and Information
U.S. President's Emergency Plan for AIDS Relief
Valid International
Walter Reed Army Institute of Research
Washington University in St. Louis
Wellcome Trust
WHO Special Programme for Research and Training in Tropical Diseases
World Health Organization
World Relief
World Vision
Wyeth

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