



USAID
FROM THE AMERICAN PEOPLE

**Report to Congress
Health-Related Research and Development for Fiscal Year (FY) 2016
U.S. Agency for International Development**

The U.S. Agency for International Development (USAID) submits this report to Congress pursuant to Public Law 111-8, the Department of State, Foreign Operations, and Related Programs Appropriations Act, 2009, which directed that:

USAID should expand collaboration with other donors and governments to develop new medicines, diagnostics and vaccines for diseases that affect the developing world. USAID is directed to continue to provide the annual research and development report to the Committees on Appropriations.

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Acronyms

3HP	Rifapentine and isoniazid once per week/three-month treatment for tuberculosis
ART	Anti-retroviral therapy
ARV	Anti-retroviral
BMI	Body-mass index
CDC	U.S. Centers for Disease Control and Prevention
CII	Center for Accelerating Innovation and Impact
COR-NTD	Coalition on Operations Research in Neglected Tropical Diseases
FDA	Food and Drug Administration
FY	Fiscal Year
HEWs	Health Extension Workers
HHS	U.S. Department of Health and Human Services
HSS	Health-systems strengthening
iCCM	Integrated community case-management
IRS	Indoor residual spraying
LF	Lymphatic filariasis
LMIC	Low- and middle-income countries
LTBI	Latent tuberculosis infection
MDA	Mass drug-administration
MDR-TB	Multi-drug-resistant tuberculosis
MNCH	Maternal, newborn, and child health
MVDP	USAID Malaria Vaccine-Development Program
NTDs	Neglected tropical diseases
OV	Onchocerciasis
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PMI	U.S. President's Malaria Initiative
RMC	Respectful maternity care
SBC	Social and behavior change
TB	Tuberculosis
UNICEF	United Nations Children's Fund
VMMC	Voluntary medical male circumcision
WHO	World Health Organization

EXECUTIVE SUMMARY

As the world's premier development agency, the U.S. Agency for International Development (USAID) finances programs to help partner countries have the resources, skills, and technologies necessary to address their most critical health-care challenges. USAID's research and development programs related to global health support the invention, refinement, and introduction of new and improved drugs, diagnostics, vaccines, tools, and approaches to treatment.

This report provides updates and results from USAID's Fiscal Year (FY) 2016 research and development program in global health. The report describes key accomplishments under priority areas for research and development identified within each health element. Some highlights from this report include the following:

Developing Tools and Approaches to Eliminate Malaria

Malaria research funded by USAID focuses on the development of new vaccines, medicines, and insecticides for the prevention and control of malaria, as well as operational research to improve the impact of malaria programs. USAID support has contributed to the advancement of three novel classes of malaria drugs (OZ439, KAF156, and DSM265), as well as another medicine, Tafenoquine, which, if approved by regulatory authorities, would be the first new medicine for relapsing malaria in more than 60 years. In Cambodia, operational research on the safety and tolerability of single, low-dose primaquine for reducing the transmission of malaria contributed to the national malaria-control program's policy recommendation to adopt this treatment in areas of the country that are moving to eliminate the disease.

Advancing New Interventions to Combat Multi-Drug-Resistant Tuberculosis (MDR-TB)

USAID is financing several clinical studies to evaluate the efficacy of shorter drug regimens to combat MDR-TB, which have the potential to increase adherence and acceptability of treatment among patients, while decreasing side-effects and transmission. Trial results from one USAID-funded study (STREAM Stage -1) will be available in early 2018, but preliminary data have already begun to contribute to the global knowledge base. The guidelines the World Health Organization (WHO) recently released on the management of MDR-TB refer to the STREAM study design in advising Ministries of Health how to determine which regimen to recommend to clinicians.

Designing More Cost-Effective Approaches to Eliminating Neglected Tropical Diseases

USAID's financing for the mapping of clusters of lymphatic filariasis in sub-Saharan Africa has enabled the more-efficient targeting of drug-administration campaigns to areas most in need. Based on favorable uptake and results, a USAID-funded study in Tanzania expanded to include Ethiopia as well. Reviewing the mapping of 45 Districts identified 42 as non-endemic, and only three as endemic and warranting treatment. Overall, the results saved millions of dollars, and improved treatment. The WHO has endorsed the new survey protocol, which will be introduced soon in other areas.

Catalyzing Innovations to Combat Emerging Pandemic Threats

As part of the Global Health Security Agenda, the 26 innovations USAID has funded range from mosquitoes infected with *Wolbachia*, a naturally occurring bacterium that prevents the transmission of disease to humans, to a predictive disease-surveillance platform that could protect vulnerable communities from becoming disease hot spots.

Accelerating Research into the Prevention and Treatment of HIV

Through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), USAID is investing in the research and development of HIV vaccines. Additionally, USAID's portfolio supports promising women-controlled methods of HIV prevention, including the dapivirine vaginal ring, a dossier for which the manufacturer submitted to the European Medicines Agency, with USAID support; the device is the first long-acting HIV-prevention method submitted for regulatory approval anywhere in the world. USAID's funding for HIV-treatment optimization led to the initiation of a pivotal trial in South Africa to compare three, different, first-line HIV-treatment regimens, including two newer anti-retroviral (ARV) drugs that could have improved profiles with respect to side-effects, efficacy, manufacturing costs, and the risk of viral resistance. USAID investments have also focused on implementation research to strengthen the delivery of PEPFAR programs.

Expanding Access to Safe and Effective Family-Planning Methods

USAID research and development in this area addresses major factors that contribute to the lack of access to voluntary family-planning methods, concerns about side-effects, inadequate or inaccurate information among couples, and poor access to reproductive health care. USAID has initiated two clinical trials to evaluate lower doses and extended duration of existing family-planning methods, which could decrease the incidence of side-effects and reduce costs for millions of users. Also, to study healthy timing and spacing of pregnancies, USAID is working in Liberia, Malawi, and Tanzania to research the effectiveness of integrating family-planning approaches with the delivery of immunizations.

Promoting Respectful Maternal, Child, and Newborn Health

Respectful maternity care addresses the treatment of women in childbirth, which has an impact on both the quality of care delivered, as well as the willingness of women to give birth in facilities. In Tanzania, a recently completed study funded by USAID documented that an intervention package that used a client-service charter to address social norms and expectations among providers and patients reduced the odds that a woman experienced disrespect and abuse in childbirth by 66 percent. In the coming year, USAID will work with the Government of Tanzania to help scale up these results to further spread respectful maternity care to neighboring areas and other partner countries.

Addressing Malnutrition by Supporting Nutritional Supplementation

USAID has funded research to improve and monitor national food-fortification programs, including an evaluation of government and private-sector capacity to add micronutrients to wheat flour and cooking oil. Through these and other efforts, the Government of Kazakhstan, a major exporter to nearby countries, adopted improved flour-fortification policies. USAID also has evaluated the financial feasibility of scaling small-quantity, lipid-based supplementation to prevent maternal and early-childhood undernutrition, which can reduce stunting, small head size, and wasting. These results have the potential to have an impact on millions of undernourished children globally.

MALARIA

Since 2000, deaths from malaria in Africa have dropped by 66 percent, which represents nearly seven million lives saved, the vast majority of them children under the age of five. The U.S. Government's unwavering commitment to ending malaria, especially since the creation of the Global Fund to Fight AIDS, Tuberculosis and Malaria in 2001 and the 2005 launch of the U.S. President's Malaria Initiative (PMI), is responsible for many of these gains. Led by USAID and implemented in

conjunction with the U.S. Centers for Disease Control and Prevention (CDC) of the U.S. Department of Health and Human Services (HHS), PMI operates in 19 of the highest-burden countries across sub-Saharan Africa, as well as in two countries and a regional program in the Greater Mekong Subregion in Southeast Asia. malaria requires , new tools and approaches, including a highly effective vaccine; novel anti-malarial drugs, innovative vector-control methods; and improved, more cost-effective approaches for delivering existing malaria interventions.

Priority 1: Develop Safe and Effective Vaccines for *Plasmodium falciparum* Malaria

A highly efficacious malaria vaccine is not yet available. The most-advanced malaria vaccine, GlaxoSmithKline's RTS,S/AS01 (Mosquirix), is a remarkable development, but it has not yet demonstrated the desired high efficacy, durability, and affordability that most experts in the field believe possible. Given the persistent need for a highly efficacious malaria vaccine, the USAID Malaria Vaccine-Development Program (MVDP) continues its efforts to develop alternative vaccine candidates with the requisite characteristics. MVDP and its partners have conducted studies with multiple vaccines that focus on preclinical and early clinical research.

Building on knowledge obtained through experience with Mosquirix, which targets malaria parasites at the sporozoite stage as they infect victims through mosquito bites, USAID is working with partners to investigate the feasibility of improved sporozoite vaccines. Studies include a planned clinical evaluation of a vaccine that contains the entire molecule upon which Mosquirix is based (since Mosquirix contains only a portion of the molecule), as well as developing novel delivery formulations that would efficiently present multiple copies of critical target portions of the molecule. In addition, MVDP is pursuing research that targets other stages of the parasite's life-cycle, including through funding a clinical trial of a liver-stage vaccine, helping to advance a cutting-edge blood-stage vaccine, and extensively analyzing parasite molecules that might be candidates for inclusion in a vaccine.

Priority 2: Develop Effective and Affordable Medicines for the Treatment and Prevention of Malaria

Resistance to artemisinin, the primary component of the most-effective combination therapies to treat malaria, has been documented in all countries in the Greater Mekong Subregion. If such resistance were to spread to, or emerge in, sub-Saharan Africa, it would devastate global malaria-control efforts. USAID contributes to drug-development through its funding for the Medicines for Malaria Venture (MMV), a non-profit foundation that works through public-private partnerships. With USAID's financing, MMV is continuing to advance the development of three novel classes of malaria drugs (OZ439, KAF156, and DSM265). OZ439 is currently in late-stage clinical trials in combination with ferroquine, a partner drug. KAF156 was shown to clear both major species of malaria parasites, and entered combination studies in 2017. DSM265, another novel anti-malarial compound that has the potential to treat malaria in a single dose, successfully demonstrated safety and efficacy in a trial in Perú.

These new treatments offer great hope for an alternative to artemisinin-based combination therapies. Tafenoquine, which could offer a single-dose cure for relapsing malaria, has completed investigational testing, and is being developed alongside a point-of-care diagnostic test to ensure its safe administration. If approved by regulatory authorities, tafenoquine would be the first new medicine for relapsing malaria in more than 60 years. Advances have also taken place in the availability of high-quality medicines for children. A pediatric formulation of the malaria treatment

pyronaridine-artesunate received pre-qualification status from the WHO, and the Global Fund to Fight AIDS, Tuberculosis and Malaria authorized the procurement of life-saving rectal artesunate for the pre-referral treatment of severe malaria in children.

Priority 3: Develop New, Effective Insecticides for Improved Vector-Control

In many African countries, resistance by mosquitoes to the most-widely available insecticides is threatening the effectiveness of both long-lasting insecticide-treated nets and indoor residual spraying (IRS) to prevent malaria.

In 2017, with support from the Innovative Vector-Control Consortium (IVCC), the WHO recommended the first new insecticide registered for public health use since the mid-1980s. The IVCC is an international public-private partnership to foster the research and development of new vector-control products and tools for public health. USAID funds the consortium's insecticide development, including to advance three novel insecticide candidates to the final stages of production by 2019. USAID's financing created two new insecticides with Bayer and Syngenta; the partners have selected lead and back-up vector-control compounds, which are undergoing evaluation for early development studies. USAID has also paid for accelerating the entry onto the market of new IRS products, which have helped to expand the use of long-lasting, non-pyrethroid insecticide IRS in Ethiopia, Ghana, Kenya, Mali, Tanzania/Zanzibar, and Uganda.

Priority 4: Improve the Implementation and Impact of Malaria-Control Programs

Through PMI, USAID funds operational research to address bottlenecks in achieving and maintaining coverage of proven interventions against malaria, while also informing malaria-control efforts as epidemiology changes, new risks and challenges arise, and new tools are introduced to combat them. Highlights from USAID's operational research in malaria from FY 2016 include studies of new interventions to improve the delivery of services to prevent and treat malaria at the community level.

In Burma, PMI-supported research found high acceptability of insecticide-treated clothing among rubber tappers, a group at high risk of malaria infection. In Cambodia, research on the safety and tolerability of single, low-dose primaquine for reducing the transmission of malaria contributed to the national malaria-control program's recommendation of this treatment in areas that are moving toward eliminating the disease.

PMI-supported research in Ethiopia and the Democratic Republic of Congo is exploring how to simplify the management of non-malaria fevers by community health workers. Such adjustments are particularly important because the reduction in malaria cases across many endemic regions has led to an increase in the proportion of non-malaria fevers seen by health workers. USAID's partners have provided the results from these studies to the WHO to assist in the updating of global guidelines on management of the sick child. Ongoing operational research in Malawi is assessing the feasibility of distributing intermittent preventive treatment for pregnant women through community health workers to help improve coverage in hard-to-reach areas.

TUBERCULOSIS (TB)

TB is the leading infectious killer in the world, and contributes to 4,000 deaths each day, more than 28,000 each week, and 1.4 million each year. There were an estimated 10.4 million new cases of TB

around the world in 2015. Exacerbating the issue, each year nearly 500,000 people become sick with drug-resistant TB strains, also called MDR-TB, including variants resistant to the two most-effective, first-line drugs, isoniazid and rifampin. The global TB community has, through the WHO's *End TB Strategy*, set an ambitious goal to eliminate TB by 2035. To reach that goal, new TB-control strategies and tools are needed to drastically reduce the annual number of new cases, and to drive an accelerated decline in the incidence of TB. With partner countries, USAID is working to build capacity among laboratorians and providers; improve patient care; strengthen diagnostic and clinical services; and facilitate the development of, and access to, improved diagnostics and drugs.

Priority 1: Improve the Treatment of Drug-Sensitive and MDR TB

The spread of drug-sensitive and MDR-TB is a global health security concern that threatens decades of progress in the prevention and control of the disease. An individual with MDR-TB faces two years of treatment; requires nearly daily visits to a health provider; and will receive 250 injections, and 15,000 pills. This regimen is difficult, and USAID is supporting clinical trials to determine the efficacy and safety of shorter regimens for the treatment of MDR-TB, under the assumption that shorter treatment with well-tolerated drugs will lead to increased adherence to treatment among patients, greater cure rates, and, eventually, reduced transmission of the disease.

The STREAM study is a clinical trial funded by USAID to confirm the efficacy and safety of a shorter TB-treatment regimen, previously tested in an observational study conducted in Bangladesh. Patients have enrolled in the STREAM Stage 1 Trial at sites in Ethiopia, Mongolia, South Africa, and Vietnam; all of them have completed treatment during the reporting period, and are currently undergoing follow-up. Final patient follow-up is scheduled for December 2017, and the results of the trial will be available in early 2018. The study has already informed policies related to the management of MDR-TB, as the guidelines the WHO recently released refer to the STREAM study design in advising Ministries of Health how to determine which regimen to recommend to clinicians. A second phase of the STREAM study is now underway, which aims to evaluate the efficacy and safety of a shorter treatment regimen that contains bedaquiline, recently approved by the HHS Food and Drug Administration (FDA). A total of 83 patients have enrolled in this study across sites in Ethiopia, Mongolia, and South Africa.

USAID is also financing the evaluation of a number of combination treatment regimens with the aim of shortening TB treatment and offering additional options for patients with extensively drug-resistant disease. The Nix-TB study is evaluating the combination of pretomanid, bedaquiline, and linezolid for the treatment of MDR-TB in patients who show additional resistance to injectables and/or fluoroquinolones. Early results show that 74 percent of patients were culture-negative for TB after eight weeks of treatment.

Beyond support for clinical studies, such as STREAM and Nix-TB, USAID is supporting community-engagement activities around clinical-trial sites. Involving communities from the beginning is an important element for the successful implementation of research activities and the translation of research findings into policies and practices.

Priority 2: Prevent the Development and Ongoing Transmission of TB

An estimated one-third of the world's population has latent TB infection (LTBI), which means these people are at risk for developing active TB disease at some point in the future. Immuno-

compromised individuals, like those who are living with HIV, are at particularly high risk of developing TB disease from a latent infection. Modeling studies have demonstrated that treating individuals with LTBI is a strategy that could lead to a rapid decline in TB incidence. New developments suggest that the treatment of LTBI with a simplified, once-a-week combination of rifapentine (P) and isoniazid (H) for 12 weeks is as effective as the conventional six-to-nine-month daily isoniazid regimen. Mathematical modelling suggests that a single course of this weekly regimen (termed 3HP, since it lasts for three months), when used at scale in settings with high transmission of TB, will achieve a significant reduction in the incidence of the disease at a population level, but these benefits could gradually wane with time. USAID is funding a study to compare the effectiveness of a single course of 3HP to two annual rounds of 3HP, to show sustained reduction in the incidence of TB in HIV-infected individuals; enrollment is ongoing in South Africa, Ethiopia, and Mozambique.

Priority 3: Build Capacity to Conduct Operational Research for Improving the Performance of TB Programs and the Management of TB-HIV Co-Infection

In conjunction with the Peruvian Ministry of Health's National Tuberculosis Program, USAID supported an operational research training course in Perú and another with the Department of Medical Research in the Ministry of Health in Burma. The aim of these courses was to teach health professionals to conduct independent operational research, and to aid them with translating findings into improved policy and practice. USAID also funded the National Research-Advisory Committee in Ethiopia to develop a national TB-research plan.

NEGLECTED TROPICAL DISEASES (NTDs)

The chronic pain, stunting, malnutrition, and disability caused by NTDs plague hundreds of millions of people around the world. USAID targets seven of the most prevalent NTDs, which together account for 80 percent of the global burden: lymphatic filariasis (LF), blinding trachoma, schistosomiasis, onchocerciasis (OV), and three soil-transmitted helminthiases. All of them are treatable, preventable conditions.

USAID works with Ministries of Health, other donors, local community organizations, and pharmaceutical companies to organize preventive campaigns for NTDs that have safely, effectively, and efficiently delivered more than two billion treatments to nearly one billion people across 25 countries, at an average cost of approximately 30 cents per person, per year. Despite tremendous progress, new tools and strategies are needed to overcome emerging challenges, and to guide both programmatic decision-making and post-intervention surveillance of the diseases.

In 2014, USAID and the Bill and Melinda Gates Foundation jointly created the Coalition on Operations Research in Neglected Tropical Diseases (COR-NTD). This coalition enables a broader group of research partners to engage, and improves global coordination across the research spectrum. It aims to remove barriers and accelerate progress toward the WHO 2020 NTD goals.

Priority 1: Support Innovative Approaches in Disease-Mapping

Information about the geographic distribution of individual NTDs is limited, particularly in areas of sub-Saharan Africa where NTDs such as Loa Loa infection (a disease of the skin and eye) could be co-endemic. Better programmatic approaches to eliminating diseases like LF and OV are urgently needed. Additionally, the mapping strategy used in the past for LF is not sufficiently robust to support programmatic decision-making in settings with very low prevalence. USAID support for the mapping

of clusters of LF in sub-Saharan Africa has enabled the more-efficient targeting of drug-administration campaigns to areas most in need. Based on favorable uptake and results, a USAID-funded study in Tanzania expanded to include Ethiopia as well. The mapping of 45 Districts identified 42 as non-endemic, and only three as endemic and warranting treatment. Overall, the results saved millions of dollars, and improved treatment. The WHO has endorsed the new survey protocol, which will be introduced soon in other areas.

Priority 2: Support Best Practices for Monitoring and Documenting Progress toward Elimination

USAID is focused on determining when to stop treating populations for NTDs by using a scientifically rigorous, patient-safety-centered coordinated protocol. These efforts increase the efficiency of programs, and reduce costs by decreasing both training requirements and the expenses of conducting surveys. USAID is comparing tools to detect antibodies, antigens, or DNA to older techniques for NTDs in USAID-supported countries to assess whether to stop mass drug-administration (MDA) programs.

In areas of overlap between LF and OV, the success of both programs is inextricably linked because of the necessity to coordinate the decision to stop MDA and initiate post-MDA surveillance. With the emerging interest in the elimination of OV in Africa, operational research is urgently needed to determine how best to coordinate decision-making with, and within, Ministries of Health. In multiple country settings, USAID is evaluating new laboratory tools to detect antibodies to both LF and OV with one combined test, to determine their feasibility and accuracy.

Priority 3: Develop Tools to Support Post-MDA Surveillance and Manage Morbidity

Although MDA programs will reduce the development of new morbidity from LF and trachoma, MDA does not address morbidities among those who are suffering from the diseases now. As such, the USAID NTD Program funds operational research with Ministries of Health to assess their countries' disease burden and how to address it.

USAID, through the COR-NTD, launched a multi-center clinical trial of doxycycline to confirm earlier, favorable results from a randomized trial that suggested effective treatment can partially reverse the debilitating limb-swelling caused by LF. Data in late 2017 will indicate whether this treatment can be incorporated into the WHO Morbidity Toolkit and potentially alleviate suffering in hundreds of thousands of people.

Priority 4: Designing an NTD Small Grants Research Program in Africa

With funding from USAID, the African Research Network for NTDs in Kumasi, Ghana, is collaborating with the COR-NTD to design the African Researchers' Small Grants Program. Collaboration with the African Research Network for NTDs provides a unique opportunity for a synergistic, concentrated, and inclusive effort to address emerging challenges that facing national programs in Africa, in line with the goals established in the London Declaration on NTDs. Four to six awards for mid- and early-career researchers will ensure the research activities are as close to the ground-level as possible, jointly guided by USAID and national NTD programs.

EMERGING PANDEMIC THREATS

The ongoing emergence and spread of diseases like H1N1 and H7N9 avian influenza, Middle East Respiratory Syndrome Coronavirus (MERS), Zika, and Ebola are clear reminders of how vulnerable an increasingly interconnected world is to zoonoses – diseases transmissible from animals to humans. Because these diseases can quickly surface and spread without warning, they pose serious concerns to public health and the economy. To protect against the potential consequences associated with emergence of a pandemic threat, USAID’s investments seek to pre-empt and combat diseases aggressively that could potentially spark future global crises.

These activities also contribute to the Global Health Security Agenda, launched in 2014 to promote a “world safe and secure from global health threats posed by infectious diseases.” Building on work that began in 2009, USAID continues to fund the surveillance of high-consequence viral families that are circulating in certain animal species in Africa and Asia. USAID couples this information with social-science research that describes behaviors and practices that evoke the spillover and spread of viruses from animals to humans, and builds the capacity of national workforces to use this information for early detection and effective responses to future threats. In all of these activities, USAID collaborates closely with HHS/CDC, the U.S. Department of Agriculture, the WHO, the World Organization for Animal Health and other international organizations.

Priority 1: Develop and Introduce Surveillance Methods to Increase the detection of Dangerous Pathogens

USAID partners continue to generate new surveillance data on microbes that are circulating in wildlife populations, with the highest priority given to rodents, bats, and non-human primate species. To date, the Agency’s partners have collected samples from more than 74,000 animals in 60 countries across Africa, Asia, and the Middle East, where new pandemic threats are most likely to occur. Using a newly developed set of protocols to detect viral pathogens, as well as a global network of laboratories, USAID’s implementers have discovered more than 1,000 novel viruses. These protocols have characterized two current pandemic threats: H7N9 avian influenza and MERS.

This information feeds into a global database ,and contributes to mapping the distribution of microbes and characterizing the risk associated with different human/animal interactions. Information is publicly available online (<http://data.predict.global>) through a suite of digital disease-detection tools that employ online informal sources to enhance real-time intelligence for emerging global health threats.

In Uganda and Malaysia, ongoing research funded by USAID investigates the diversity of pathogens across different types of development, including urban, peri-urban, and undeveloped areas. This study will help clarify the impact of human activity on the diversity of wildlife and microbes, and provide initial insight into how those settings provide new opportunities for animals and humans to interact.

USAID partners also generate surveillance data in China and Vietnam on influenza viruses that are circulating in farm animals, including swine, poultry, and wild birds. This information sheds light on the distribution, diversity, seasonality, and evolution of a family of viruses that has caused four pandemics in the past century.

Priority 2: Develop and Test Methods to Improve the Understanding of How Human Behavior Contributes to the Risk of Emerging Diseases

In areas that represent a high risk for the emergence of pandemic threats, specific practices of communities and industries (such as the oil, gas, and mining sectors) can put people in danger. By reviewing the “hotspot” maps of high-risk areas with new datasets, USAID’s implementing partners have found a relationship between the risk of emerging disease, human population growth, and wildlife diversity. New high-resolution maps that provide subnational information on the highest-risk areas show the underlying drivers of diseases vary by region, and indicate that new diseases emerge primarily from changes in land use, agricultural intensification, and associated secondary factors (e.g., the hunting, butchering and consumption of wild animals, known as “bushmeat”) in locations with the most zoonoses. To date, the most-comprehensive and detailed information available on the emergence of zoonotic diseases demonstrates that the highest risk of disease transmission is associated with human and domestic animal interaction with wildlife, including the preparation raiding of crops by wildlife. These data help national governments and international partners prepare for pandemics by guiding surveillance, and the development of strategies to prevent and control zoonoses.

USAID also funds in-depth research to locate high-risk populations, and identify social preferences and practices linked to risky contact between humans and animals. For example, USAID projects continue to use prior characterization of the trade in wild-animal meat and the infrastructure that exists in markets in the Democratic Republic of Congo, Indonesia, the Lao People’s Democratic Republic, and Vietnam. This enables an understanding of the quantity and types of wild-animal meat that move through markets and the value chain, as well as how people handle the meat. Ultimately, this information will ease the development and testing of interventions that reduce risk.

HIV/AIDS

USAID’s HIV/AIDS research priorities, financed by PEPFAR, are intended to maximize the reach of technically sound, cost-effective, and sustainable interventions to serve the U.S. Government’s strategic goal of sustained control of the epidemic. Because more than half of the 36.7 million people living with HIV worldwide are women and girls, the Agency also emphasizes the development and introduction of new, women-initiated prevention tools.

Priority 1: Strengthen the Programmatic Evidence Base for the Prevention, Care, and Treatment of HIV/AIDS to Achieve Epidemic Control

USAID funds the evaluation of how novel interventions can go to scale in real-world settings, by collaborating with local researchers, research institutions, and program implementers, as well as by ensuring the full use of research data to inform policies and programmatic decision-making. USAID assists Ministries of Health with strategic planning to achieve higher coverage of voluntary medical male circumcision (VMMC), and has funded feasibility studies to test new approaches to preventing and caring for the disease, such as HIV self-testing and community-based HIV-treatment services. USAID has also worked to measure the cost-effectiveness of different “test-and-start” strategies (i.e., the immediate initiation of HIV treatment for those newly diagnosed with HIV), including the assessment of community-based service-delivery and the identification of optimal treatment outcomes for key populations.

USAID-funded research has recently demonstrated that the early diagnosis of HIV in infants (within two weeks of birth), followed by immediate treatment, is feasible and highly acceptable to mothers and healthcare workers. USAID has also partnered with the Joint United Nations Programme on HIV/AIDS (UNAIDS), the Global Network of People Living with HIV/AIDS, and the International Community of Women Living with HIV to update *the People Living with HIV Stigma Index* – a tool that measures trends in stigma and discrimination experienced by people who are living with HIV.

Priority 2: Accelerate the Development and Clinical Testing of Novel HIV Vaccine Candidates, and Strengthen the Global Capacity for Vaccine Research

Since 2001, USAID has supported research and development¹ into HIV vaccine candidates. New collaborative initiatives that use emerging technologies are generating evidence about key components of the immune system that are responsible for preventing or controlling HIV infection.

ADVANCE, a new project funded by USAID and led by the International AIDS Vaccine Initiative, plays a unique role in the investigation of by focusing on the immunological characteristics of populations in sub-Saharan Africa, the viral-variants across the globe, and the realities of the epidemic where it is most severe, including in key PEPFAR priority countries. The ADVANCE project has forged broad-reaching strategic partnerships, and strengthens scientific leadership as well as laboratory and clinical-trial capacity across sub-Saharan Africa. At the core of the ADVANCE project is the effective training of African scientists and the transfer of novel technologies to advance the understanding of HIV pathogenesis. The project funds four Phase I HIV-vaccine trials that test novel approaches to protect against the disease. Later-stage efficacy trials will begin in 2018, which will further inform the design of future candidate vaccines.

To complement the scientific efforts in ADVANCE, USAID pays for in-country policy and communications work. These activities inform national policy-makers on the importance of HIV research, while encouraging domestic investment in research and development into HIV vaccines. The engagement of civil society, particularly in affected communities, is central to these efforts, and leads to optimal accountability, acceptability and transparency of clinical trials.

Priority 3: Develop, Test, and Introduce Microbicides for Women to Reduce the Risk of Infection with HIV

USAID continues its response to the disproportionately high burden of HIV in African women, especially adolescent girls and young women, by financing the development of microbicides – biomedical products that enable women to protect themselves from HIV infection. Building on the promising results in 2016 from two Phase III efficacy trials of the dapivirine vaginal ring, USAID has funded multiple activities to help prepare for the successful regulatory approval of the device and its introduction onto the market. USAID invested in an ongoing, open-label, follow-on study (the DREAM Study) to collect additional safety data on the dapivirine ring; investigate real-world options for delivering the product, and evaluate if correct and consistent use of the device will increase as women understand its safety and efficacy. With USAID support, in June 2017 the dapivirine ring became the first long-acting, female-controlled HIV-prevention product submitted for regulatory review and approval for licensure when the manufacturer, QPharma of Sweden, submitted a dossier to the European Medicines Agency.

¹ <https://www.usaid.gov/what-we-do/global-health/hiv-and-aids/resources/news-and-updates/usaids-marks-15-year-partnership>

Simultaneously, driven by the need for other products that are feasible for delivery and use in resource-limited settings, USAID funds the development of other innovative HIV-prevention technologies. These include more-acceptable and less-expensive formulations of oral pre-exposure prophylaxis, biodegradable implants for the long-term delivery of ARVs, patches that rapidly deliver ARVs through the skin for a month or more of protection, products that would prevent both HIV and unintended pregnancies, and suitable candidates for on-demand protection.

In addition, the USAID-managed Microbicide Product-Introduction Initiative focuses on accelerating the introduction of, and access to, oral pre-exposure prophylaxis, the dapivirine vaginal ring, and other products in the pipeline. These activities in PEPFAR countries address program-planning, impact-modeling, policy-development, demand-generation, service-delivery, gender issues, and concerns about viral resistance to ARVs.

Priority 4: Improve HIV Treatment through the Optimization of ARVs

USAID finances the optimization of anti-retroviral therapy (ART) to make it safer, simpler, and more affordable. Many low- and middle-income countries (LMIC) strive to transition to new, lower-cost ARV drugs in ART programs, which could potentially save an estimated \$1 billion in health budgets by the end of 2025.

A key accomplishment from USAID's support for ART optimization within the reporting period was the successful initiation of a randomized trial in South Africa to compare three, different, first-line HIV-treatment regimens to one another. This included a current, WHO-recommended, first-line regimen used by most patients in LMIC, and two other, first-line regimens that contain dolutegravir and tenofovir alafenamide fumarate in combination with other ARVs. These two relatively newer ARVs are expected to have improved profiles with respect to side-effects and toxicities. They also lower manufacturing costs with less risk of viral resistance. The trial, co-funded by UNITAID, will inform future global and country ART guidelines.

VOLUNTARY FAMILY PLANNING AND REPRODUCTIVE HEALTH

An estimated 214 million women in developing countries want to space or limit births, but are not using a modern method of family planning. Factors that contribute to this unmet need include concerns about side-effects, inadequate or inaccurate information among couples, and poor access to voluntary services.

Priority 1: Refine, Develop, and Introduce New Contraceptive Methods

In 2016, initial work finished on the development of a biodegradable microneedle injection technology for progestin contraceptives. Two complementary technologies underwent testing for proof-of-concept in the laboratory, and are moving into the next stages of development with leveraged financing from USAID and the Bill and Melinda Gates Foundation.

Additionally, pre-clinical development funded by USAID continued on multi-purpose technologies designed to prevent unintended pregnancy and protect against HIV and, potentially, other sexually transmitted infections. In collaboration with the U.S. National Institutes of Health within HHS, USAID financing allowed a multipurpose prevention vaginal ring that contains dapivirine and levonorgestrel to enter clinical testing in mid-2016.

USAID also initiated two clinical trials to refine existing methods of contraception. The studies will evaluate the safety and effectiveness of lower doses of Depo-Provera and extended re-injection intervals of Sayana Press. The outcomes of these studies could make these safe and effective methods of contraception more acceptable and affordable to millions of users.

As new methods, such as the hormonal intrauterine device and the SILCS diaphragm, are introduced in several countries, USAID continues to coordinate with donors, manufacturers, and implementing partners to assess and document efforts to inform the scale-up of these products.

Priority 2: Improve and Expand Access to Voluntary Family-Planning Methods in Developing Countries

USAID funds research to address social norms related to unintended pregnancy and sexual and reproductive health among youth. Project interventions, such as working with faith communities and religious leaders, promote community-level change to support voluntary family planning and the healthy timing and spacing of pregnancies. In addition, Agency partners provide technical assistance to organizations that are scaling up approaches with husbands in Niger and grandmothers and senior women in Sénégal. Globally and regionally, USAID-funded projects work with donors, researchers, and implementing organizations to share tools and approaches on research and practice into community-level normative change.

USAID partners are also researching the association between knowledge of the fertile period and contraceptive use. Research will demonstrate the effectiveness of community-based platforms to improve fertility-awareness and the voluntary adoption of family planning among marginalized groups in Nepal. In Rwanda, USAID-funded research has shown that including behavior-change messaging on family planning, gender, and maternal and child health in radio programs increased the knowledge of pregnancy risk in communities, and improved supportive norms around the use of family planning. To reach groups with high unmet need directly with information and services, USAID is testing the efficacy and effectiveness of an app-based algorithm for family planning.

In post-conflict communities in northern Uganda, USAID has financed implementation research to test and scale up a package of interventions based on participants' life-stage to support community-engagement on gender equity and reduce violence. Results indicated improved uptake of voluntary family planning gender-equitable attitudes; and communication and decision-making by couples, particularly among newly married and parenting adolescents. The scale-up phase demonstrated that local governments, NGOs, and community-based organizations integrated the activities as part of their ongoing interventions, while maintaining quality. USAID is funding the adaptation of these interventions to an urban setting with high unmet need.

In Benin, USAID has financed implementation research to test a social-network diffusion approach, shown to increase the voluntary use of modern methods of contraception. USAID funded the scale-up of this technique, and demonstrated organizations could deploy a package of interventions while maintaining their quality.

Priority 3: Develop and Introduce Effective, Scalable Service-Delivery Models to Increase the Healthy Timing and Spacing of Pregnancies

USAID provides funding to the WHO to coordinate the Global Early Adolescent Study in collaboration with research institutions around the world. This study has conducted qualitative research with adolescents aged 11–14 years in 15 high-, middle- and low-income countries to better understand the life circumstances and social influences of this age group as they form gender norms and adopt sexual/reproductive-health behaviors. The qualitative research provides important insights into the types of age- and culturally appropriate programmatic and policy interventions that are needed, and has enabled the development of a suite of measurement tools, now being applied in the implementation of longitudinal research in five countries.

To address the unique needs of first-time parents, USAID finances research in Nigeria on the healthy timing and spacing of births, and the uptake of postpartum family planning to prevent rapid, repeat pregnancies among 15–24 year olds. The studies also focus on male-engagement and promoting positive parenting behaviors. Also in Nigeria, research funded by USAID demonstrated that community health workers can effectively and safely insert and remove contraceptive implants, which proves that task-sharing to promote greater access to voluntary family-planning methods in at the community level is feasible. In Liberia, Malawi, and Tanzania, USAID supports research on the effectiveness of integrating family-planning approaches with immunizations to improve the timing and spacing of pregnancies by mothers of young children.

USAID has also funded formative research on exclusive breastfeeding and the lactational-amenorrhea method in Tanzania. Results showed that most women wait until their menses returns before considering contraceptives, and most were not exclusively breastfeeding at six months. These findings informed the design of an intervention study to promote exclusive breastfeeding and the lactational-amenorrhea method to reduce unintended, closely spaced pregnancies.

MATERNAL, NEWBORN AND CHILD HEALTH (MNCH)

USAID’s applied research into MNCH , as well as our implementation research and utilization activities, follow a managed evidence-to-use process. USAID pays for the development and adaptation of tools, approaches, and interventions to help reduce newborn, child, and maternal mortality in partner countries, and facilitates their use. The Agency identifies and addresses critical gaps by working in partnership with researchers, policy-makers, and implementers, while especially emphasizing the leadership role of LMIC institutions and practitioners. When possible, this process also involves embedded research within service-delivery platforms, continuous knowledge-management, and cross-country learning to accelerate and enhance timely uptake. USAID and its MNCH implementers work across the continuum of care from the community through the facility level.

Priority 1: Improve the Access and Use of Evidence-Based Approaches for Quality MNCH Care

USAID achieves our greatest impact in improving quality by using implementation research embedded in real-world settings. The Agency works to develop solutions for both demand- and supply-side problems, such as changing the behaviors of clients and providers, as well as instituting approaches to better provide care. This has included funding evaluations of service-integration; investigations into the role of quality performance-based incentives; and studies to overcome gaps in

clinical services and critical maternal and child health commodities; as well as advance respectful maternity care (RMC).

RMC addresses the mistreatment by health workers of women in childbirth, which has an impact on both the quality of care delivered and the willingness of women to give birth in facilities. In Nigeria, USAID-funded research has documented physical abuse, physical restraint to a delivery bed, detainment, and verbal abuse of mothers in labor. Prior USAID-financed research in Kenya has resulted in an evidence-based national effort to advance RMC. In Tanzania, a recently completed study funded by USAID documented an intervention package that reduced by 66 percent the odds of that a woman experienced disrespect and abuse in childbirth. In the coming year, USAID will work with the Government of Tanzania to adapt these results and help catalyze further spread of RMC to other partner countries. The findings of these studies, along with other implementation-research efforts, point to the need to identify social and contextual norms and devise multi-faceted country-specific interventions to solve this problem.

Possible serious bacterial infections in newborns and young children, including sepsis, remain a leading cause of under-five mortality. USAID is working with African and Asian countries to adapt a new, WHO-endorsed outpatient treatment that uses amoxicillin and gentamicin in settings in which referral to hospitals is not possible. In Ethiopia, national policies for community-based newborn care call for Health Extension Workers (HEWs) to administer antibiotics and refer sick young infants with possible serious bacterial infections to a health center; the Ministry of Health recommends that HEWs treat only when referral is not accepted or possible. USAID-funded research assessed whether caregivers who accepted referrals complied with them, and found that only 38 percent took their sick young infants to a higher health facility within 48 hours of the referral. The finding of highly variable quality of care because of gaps in parents' understanding and the destination facilities' adherence to the treatment protocol, helped spur the Ethiopian Government's to strengthen its two-way referral system at the primary health-care level, and to develop mechanisms to enforce adherence to policy. Capitalizing on these improvements in care in Ethiopia, USAID partners held a co-design workshop in Zambia with Ministries of Health from nine countries that want to advance this simplified sepsis regimen by addressing gaps in policy and implementation. In the year ahead, USAID will be collaborating with the WHO, the United Nations Children's Fund (UNICEF), and the Bill and Melinda Gates Foundation to work with early-adapter countries.

In Kenya, a USAID-funded study of integrated community case-management (iCCM) of child illnesses evaluated the feasibility, success factors, and challenges of using community health volunteers to provide treatment in the Bondo Sub-County community in Siaya County. The findings showed that when community health volunteers received training in iCCM, drugs and supplies, and proper supervision, they effectively treated children with malaria, diarrhea, or suspected pneumonia at the community level, and referred cases for further care in a timely manner. The proportion of caregivers in the intervention community units who first sought treatment from a community health volunteer increased significantly. During the past year, these findings informed the scale-up of iCCM in the remaining five Sub-Counties in Siaya and in the neighboring County of Migori.

A seven-country case study financed by USAID of illness-recognition and care-seeking behaviors for maternal and newborn complications examined household, community, and health system-level factors that influence delays in life-saving care. Findings indicated that the recognition of maternal

symptoms and decision-making to seek care is much better and faster than for newborns, but patterns of care-seeking vary. In their quest to find appropriate treatments, families seek care from multiple points, and repeatedly experienced perceived and actual poor quality of care, which suggests a reason for further delay. Taken collectively, the findings point to a need for better and more-nuanced differentiation of messages for mothers, children, and newborns directed at different influencers. Poor-quality and unresponsive care at facilities underscores the need for communities to receive counseling on the most-likely reliable sources of care for mothers and newborns who are experiencing complications. Efficient and functional referrals influence care-seeking, and are critical for ensuring access for mothers and their children to appropriate levels of care. In the coming year, USAID anticipates building on this learning through the development and testing of new interventions.

NUTRITION

Nutrition is one of the most critical factors for ensuring a healthy life. Hunger and undernutrition lead to more child deaths annually than any disease, and malnourished children tend to start school later, are more likely to drop out of school earlier, and earn less throughout their lifetimes. USAID's investments in nutrition are aimed at improving nutrition and the physical, mental, and socio-emotional development of individuals in vulnerable populations, particularly in the 1,000 days between pregnancy and a child's second birthday, when an optimal supply of food, health, and care plays a major role in the foundation of lifelong health.

Priority 1: Strengthen and Expand the Evidence Base on Integrated Multi-Sectoral Approaches to Improve Nutrition Outcomes, Including by Reducing Child-Stunting, Anemia in Mothers and Children, and Micronutrient Deficiencies

Causes of anemia are complex; therefore, there is a need to introduce simple, low-cost, and reliable methods for diagnosing its causes and monitoring the impact of interventions to reduce it. To facilitate the establishment of government-led national anemia working groups, USAID has funded national anemia landscape analyses. These groups led to the creation of evidence-based, multi-sectoral national anemia action plans. In Uganda and Sierra Leone, USAID investments have fostered the coordination of anemia support across sectors. USAID's programs have created a global, integrated community of practice to raise awareness about preventing anemia, to coordinate efforts, and to share research on effectively addressing and measuring the condition.

USAID has also financed data-collection on the effects on women's empowerment of nutrition schools for farmers. Using the Women's Empowerment in Agriculture Index, USAID partners found that women who participated in a program to educate farmers in Bangladesh about nutrition were more empowered than those who did not. The Bangladeshi Ministries of Health and Agriculture collaborated to enhance the program by facilitating training in nutrition for Government staff, and by employing stories and videos to lead activities to promote social and behavior change (SBC) within communities. Continued research and monitoring of the results of women's participation in the nutrition schools in Bangladesh are underway.

USAID partners also conducted research to advocate for, improve, and monitor national food-fortification programs. When relatively well-developed factories manufacture processed foods, and those foods are accessible and frequently consumed by target populations, fortification is an effective and cost-efficient manner to address micronutrient inadequacies. USAID-funded assessments evaluated the capacity of governments and industries to increase the supply of micronutrients through

fortifying wheat flour and cooking oil in Central Asia, Afghanistan, and Pakistan. This research assessed and discussed the harmonization of standards for fortification, support for adopting legislation, and the strengthening of quality-control and enforcement systems. Cost-benefit analyses of wheat-flour fortification funded by USAID have taken place in several countries in the region, which resulted in increased flour-fortification in Kazakhstan, an exporter of fortified products throughout the region.

Similarly, USAID financed and guided a methodology review to quantify iodine levels in iodized salt, and several low-cost and effective methods are available as a result. In collaboration with UNICEF, USAID and its partners are reviewing the indicators of success of these programs to ensure the fair assessment of progress and achievements of salt-iodization programs, which have kept iodine deficiency, the most-important preventable cause of intellectual disability, under control.

Priority 2: Support Implementation Research for Improved Dietary Diversity and Quality

To assess the financial feasibility of scaling up small-quantity, lipid-based nutrient-supplement interventions to prevent maternal and early childhood undernutrition, USAID financed an analysis of the cost-effectiveness of nutrition interventions. Small-quantity, lipid-based nutrient supplements in the diet targeted at women during pregnancy and six months postpartum and children between six and 24 months reduced newborn stunting, wasting, and small head size. The study also examined the cost-effectiveness of promoting combinations of micronutrient-intervention and related policies in low-income countries. These pioneer studies have the potential to promote interventions to improve the lives of millions of individuals with inadequate diets worldwide.

USAID also funded and promoted a cost-analysis in Uganda of the distribution of micronutrient supplements in the form of powders. Many organizations are introducing these products in various countries, but the programmatic requirements have not received sufficient attention. Findings suggest that even before considering efficacy, research focusing on economic feasibility and population coverage is important.

USAID recently financed research and activities in Nepal to assess the feeding practices of infants and young children. These behaviors are particularly poor in rural areas of Nepal, so USAID partners conducted formative research to inform the implementation of an integrated activity, including SBC. The study led to implementation and monitoring focused on the consumption of food from animal sources, nutrition for sick children, hand-washing behaviors, and women's empowerment. A package for implementation at scale will roll out nationally in food-secure and -insecure areas in Nepal. The package will include SBC, nutrition-assessment and counselling support; adolescent health; governance; family planning; and water, sanitation and hygiene components.

Priority 3: Develop, Refine, and Expand the Use of State-of-the-Art Measurement Tools for Nutrition Programs and Policies

Determining body-mass index (BMI) is an inexpensive, reliable way for health workers to identify malnutrition in children over five years of age; adolescents; and non-pregnant, non-lactating adults. However, BMI can be challenging to assess accurately in low-income settings. Therefore, USAID financed the creation of a BMI wheel for healthcare workers to calculate quickly the BMI and BMI-for-age among these populations. The BMI wheel enables more-accurate BMI measurements, and eliminates the need to calculate or cross-check reference charts, which significantly reduces the time

burden for service-providers. USAID partners printed and distributed BMI wheels for use by facility-based service-providers in Côte d'Ivoire, Malawi, Tanzania, Uganda, and Zambia. Further dissemination efforts are planned, both in person and virtually.

HEALTH SYSTEMS

Research into the strengthening of health systems (HSS) includes any method of study that analyzes the impact of health policies and practices on the performance of health institutions, and the impact that performance has on health outcomes. HSS often employs implementation research, which assesses the real-time impacts an intervention has on surrounding systems, and incorporates application of the findings into study design. USAID is actively building the HSS evidence base to inform better decision-making by policymakers in LMIC to improve health outcomes.

Priority 1: Measure the Progress and Trace the Impacts of HSS Investments

The connections between health systems and health outcomes are intuitive, but establishing a direct linkage is often complicated; however, USAID has worked with UNICEF to estimate the number of lives that investments in HSS interventions can save. By focusing on building strong, resilient public and private health systems, USAID investments could save the lives of 5.6 million children and 260,000 women from 2016–2020. To calculate these numbers, UNICEF conducted a full literature review of HSS impacts on health outcomes, and assembled an expert review panel to validate and quantify the data. The findings are now part of the UNICEF Equitable Strategies to Save Lives Tool and the Johns Hopkins University Lives Saved Tool to model the number of lives saved from these interventions. USAID published the results and methodology in the *Acting on the Call Report 2017: A Focus on Health Systems*.²

Over the last several years, USAID has worked to develop and pilot a framework and metrics to measure pharmaceutical-systems strengthening and performance that identifies priority areas for investment, and measures progress over time. Strong pharmaceutical systems are important for controlling and treating diseases, and can provide economic benefits. USAID funded a study in Kenya to measure the economic cost of non-adherence by patients to TB medicines that found increased length and severity of illness, death, disease-transmission, and drug-resistance when infected people did not complete their treatment regimens. Ensuring the availability of quality medicines saved an estimated 7,000 lives; prevented the development of more than 1,000 cases of drug-resistant TB and more than 400 new infections; and saved more than \$113 million.

Priority 2: Identify Effective Interventions That Integrate Two or More HSS Functions

Health-system functions³ interrelate and overlap, as changes in one often have effects on others. USAID partners study interventions that integrate two or more health-system functions to improve the efficiency and/or effectiveness of the elements of a whole health system.

An example is USAID's legacy of investing in quality-improvement research, which integrates learning across health-system functions to understand the performance of health workers and its effect on health outcomes for patients. USAID financed a four-year study in Tanzania to identify the factors

² <https://www.usaid.gov/actingonthecall/2017-report>

³ The six internationally recognized health-system functions are health finance; health governance; health information; service-delivery; human resources for health; and products, vaccines and medical technologies.

that influence the engagement of health workers and its impact on service-delivery. The study found four key characteristics of an engaged health care worker: 1) being a change agent; 2) job satisfaction; 3) accountability; and, 4) equitable and client-centered care. USAID continues to incorporate these characteristics in programs that target human resources for health, health governance, and improvement in service-delivery.

In Uganda and Swaziland, USAID used funding from PEPFAR to commission a similar exercise⁴ focused specifically on the performance of community health workers. These studies contribute to research on two domains of their effectiveness: performance and productivity. Key factors for improved performance in the studies include increased salaries, confidentiality training, and access to necessary supplies. The relationship between performance and productivity was less clear, which suggests that interventions to improve the effectiveness of community health workers should treat the domains separately, since improvements in one were not necessarily associated with improvements in the other. Ministries of Health and other implementers can incorporate these findings into health programs, and they will contribute to the collection of quality-improvement evidence supported by USAID, such as a forthcoming quality-improvement casebook that applies field research by teaching practitioners how to improve the quality of care.

SOCIAL AND BEHAVIOR CHANGE (SBC)

SBC programming is a strategic priority for USAID, as it has the power to catalyze both shifts in socio-cultural norms and sustained changes in collective and individual behaviors. In addition, it is an essential element of effective health programming, because it shapes not only demand for, and the correct use of, products and services, but also the practice of preventive behaviors outside the health system. Recent years have seen significant changes in behavioral programming, from transformative shifts in countries' communication landscapes to a growing interest in newer approaches that have an impact on individual behavior through attention to structural and environmental factors. SBC research helps to provide current and actionable evidence to improve the impact and cost-benefit of USAID's health programming.

Priority 1: Rapidly and Rigorously Test New SBC Approaches

Further research is needed on a range of SBC approaches, including behavioral economics, performance-based financing, and other domains that can affect individual behavior through attention to structural and environmental factors. An Interagency Agreement with the Office of Evaluation Sciences (OES) of the General Services Administration (GSA) enabled USAID, host-country governments, local organizations, and community counterparts to implement and evaluate with rigor the SBC interventions and activities that support USAID health priorities. GSA/OES combines academic expertise in social and behavioral sciences across a variety of disciplines with experience in rapidly testing program impacts in complex settings. Ongoing studies are embedded in current USAID health programming in Nigeria (preventing malaria in pregnancy and education on voluntary family-planning services) and Ethiopia (HIV-testing and adherence to ARV treatment).

Priority 2: Better Understand and Affect Normative Change to Support Healthy Behaviors

Underlying social norms have a considerable effect as either hindrances or enablers of practicing healthy behaviors. Ongoing global research financed by USAID focuses on understanding and

⁴https://www.usaidassist.org/sites/assist/files/assist_improving_chw_performance_and_productivity_mar2017_usltr.pdf

fostering social norms and normative change around age- and culturally appropriate sexual and reproductive health for adolescents, specifically the voluntary use of modern family-planning methods, and achieving the healthy timing of first and subsequent pregnancies. This project replicates and scales up social-norm interventions, and applies implementation-science principles to explain what makes interventions effective and sustainable, at scale, and in real-world contexts. It also assists in the monitoring and evaluation of community-centered SBC interventions that can be implemented widely. Collectively, this work helps to ensure that future programming will be both effective and far-reaching.

In the area of HIV/AIDS, changing social norms and expectations around circumcision can help to increase access to VMMC for young men and boys. A multi-country study funded in South Africa, Tanzania, and Zimbabwe led to better understanding the quality of counseling within adolescent VMMC services. Increased uptake of VMMC could help avert 3.36 million new HIV infections by 2025.⁵ Additionally, current evaluations of USAID’s HIV/AIDS SBC programming include stigma-reduction strategies in Mozambique and male-engagement strategies for improving the initiation of treatment and retention of HIV-positive patients in care in Côte d’Ivoire.

Priority 3: Develop More-Rigorous Programming and Evidence Standards for SBC

USAID is part of a WHO-led partnership that is improving how to build, report, assess and apply evidence for SBC and community-engagement interventions. These efforts include reviewing and strengthening the WHO’s guideline-development process; the partners are preparing the results for publication.

Strategically building on the existing evidence base, USAID is working to prioritize a global research agenda for SBC and community-engagement interventions for MNCH, by providing specific guidance on priorities to inform decisions and investments. A global survey of researchers, practitioners, Ministry of Health officials, United Nations agencies, donors, NGOs, and others solicited research topics for MNCH that will soon undergo final prioritization.

USAID recently completed a first iteration of standards on complete and accurate reporting on the design, implementation, and monitoring-and-evaluation processes for our funded programs in SBC. These standards will facilitate the replication of research and programs, ensure fidelity in reporting, and help global efforts to collect and synthesize findings. SBC programming is critically linked to its context, but contextual information is often missing from reports and journal articles. The program-reporting standards will help ensure that necessary information is systematically captured across programming, and work to fill gaps in existing literature and reports.

Priority 4: Improve the Cost-Benefits and Impact of SBC

Through its funded research, USAID continues to identify design practices that support behavioral impact and improve cost-benefits within SBC programming. Of particular interest are approaches that allow implementers to better select communication channels, segment audiences more effectively, and identify priority behaviors for interventions. Another project financed by USAID is applying predictive audience-segmentation approaches in Côte d’Ivoire and Niger to better tailor SBC interventions for increased impact. Finally, secondary analysis of several large datasets from Nigeria has allowed USAID and its partners to understand “gateway behaviors” – those that have the potential

⁵ <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001132>

to affect multiple health outcomes (e.g., attendance at antenatal care and couples' communication), which can contribute to programmatic efficiencies and cost savings.

CENTER FOR ACCELERATING INNOVATION AND IMPACT

Whether a life-saving idea lives up to its promise is contingent upon its introduction in a timely fashion, and its distribution and use at scale. The process of bringing to market and adopting global health innovations, however, can be lengthy, complex, and resource-intensive. As a result, new products or techniques often take years, and sometimes decades, to reach the people who need them most.

To overcome these challenges, USAID established the Center for Accelerating Innovation and Impact (CII) within its Bureau for Global Health, which takes a business-minded approach to fast-tracking the development, introduction, and scale-up of interventions that address the world's most-important health challenges. USAID, through CII, invests in the most-promising ideas and novel approaches, and uses forward-looking business practices to cut the time it takes to transform discoveries in the laboratory into impact on the ground. CII works via three channels: 1) catalyzing innovation; 2) accelerating the introduction and scale-up of priority global health innovations; and, 3) identifying cutting-edge practices.

Priority 1: Catalyze Innovation

USAID solicits and jump-starts game-changing innovations through novel approaches like the Grand Challenges, which ask the brightest minds around the world to submit innovative, creative, and multi-disciplinary proposals to tackle age-old global health problems head-on. Since 2011, USAID and its partners have cultivated a pipeline of over 150 innovations, in areas from improved MNCH to enhanced responses, to outbreaks of diseases like Ebola and Zika, to strengthened health supply chains, and financed them on their path to deliver health impact. The Saving Lives at Birth Grand Challenge, for example, is a highly regarded international partnership that has leveraged \$80 million from other donors, and sourced a robust pipeline of 107 potentially radical innovations from across the world.

More recently, as the threat of Zika grew at an alarming rate in 2016, USAID launched Combating Zika and Future Threats: A Grand Challenge for Development. This effort called upon global innovators to generate cutting-edge approaches to fight Zika, and to help strengthen the world's ability to prevent, detect, and respond to future outbreaks of infectious disease. Applicants submitted nearly 900 ideas; after a rigorous selection process, USAID used FY 2015 funds to invest in 26 solutions, and has provided critical financial, human-centered-design and business-strategy support to promote the development, testing, and introduction of these technologies. The innovations range from mosquitoes infected with *Wolbachia*, a naturally occurring bacteria that prevents the transmission of diseases to humans, to a predictive disease-surveillance platform that could protect vulnerable communities from becoming disease hot spots. In Medellín, Colombia, Monash University's Eliminate Dengue Program is scaling up the deployment of *Wolbachia*-infected mosquitoes, a potentially self-sustaining intervention that could complement and enhance other vector-control approaches; the effort has shown sustained coverage over a community of 250,000 people. This project is a partnership between USAID, the Government of the United Kingdom, the Bill and Melinda Gates Foundation, and the Welcome Trust.

Priority 2: Accelerate the Introduction and Scale-up of Priority Global Health Innovations

To accelerate the impact of priority global health innovations, USAID, through CII, pairs successful private-sector principles and practices with decades of experience in development. This includes strategic planning for the introduction and scale-up of new products, market-shaping, and innovative financing.

This past year, CII and the USAID Office of HIV/AIDS, along with the International Partnership for Microbicides, financed qualitative research to understand the needs of potential users of the dapivirine vaginal ring (mentioned above) in Uganda and South Africa. USAID-funded researchers spoke with young women, as well as their influencers, including young men, health providers, and community leaders, to better understand their lives, needs, and behaviors, and how the dapivirine ring fits into them. The human-centered design concepts and tools developed through this study include communication approaches to 1) increase understanding and receptivity of the ring; 2) support young women as they use the ring voluntarily; and, 3) build communities around awareness and use of the ring. These results will shape demonstration projects and open-label studies in Uganda and South Africa, and inform planning for the global launch of the anticipated new product. A synthesis of this research appears in a publication entitled, *The Dapivirine Ring Design Guide: Human-Centered Design Research to Increase Uptake and Use*.⁶

Priority 3: Identify Cutting-Edge Practices

CII identifies and applies cutting-edge practices to its work, and shares these with the broader global health community to develop and scale innovations rapidly for impact. To ensure USAID is applying the best evidence to its own work, and also disseminating these shared learnings, CII has developed a dynamic suite of hands-on tools that capture best practices, private-sector principles, and decades of global health experience. These tools support improved planning for the introduction and uptake of new products; highlight lessons and practices for shaping inefficient markets; and match challenges along the healthcare continuum with relevant, innovative financing solutions.

As an example, CII recently released *Investing for Impact*,⁷ an interactive and educational report designed for USAID staff and development practitioners. *Investing for Impact* examines trends in development finance, and highlights the ways in which USAID is leveraging private investment and applying non-traditional approaches to financing global health.

⁶https://www.usaid.gov/sites/default/files/documents/1864/V15_original_new.compressed_508_fixed_final.pdf

⁷ <https://www.usaid.gov/sites/default/files/documents/1864/investing-for-impact-aug2017-508.pdf>

Appendix I: Funding for Health Research Priorities

Health Area	Priority Areas	FY 2015 Obligated Funds	FY 2016 Expected Funds
Malaria	1. Develop safe and effective vaccines for Plasmodium falciparum malaria	\$ 7,100,000.00	\$ 7,100,000.00
	2. Develop effective and affordable medicines for the treatment and prevention of malaria	\$ -	\$ 1,000,000.00
	3. Develop new effective insecticides for improved vector control	\$ 2,000,000.00	\$ 2,000,000.00
	4. Improve malaria control program implementation and impact	\$ 2,655,219.00	\$ 2,877,819.00
	Total	\$ 11,755,219.00	\$ 12,977,819.00
Tuberculosis	1. Improve treatment of drug-sensitive and multidrug-resistant TB	\$ 9,157,013.00	\$ 10,377,524.00
	2. Prevent development and ongoing transmission of TB	\$ 3,842,987.00	\$ 5,315,463.00
	3. Conduct, and build capacity and infrastructure to conduct, operations research	\$ 2,238,849.00	\$ 1,985,000.00
	Total	\$ 15,238,849.00	\$ 17,677,987.00
Neglected Tropical Diseases*	1. Coalition for Operational Research on NTDs	\$ -	\$ -
	2. Drugs for Neglected Diseases Initiative Macrofilaricide Program	\$ -	\$ -
	Total	\$ -	\$ -
Emerging Pandemic Threats	1. Develop and introduce surveillance methods to increase pathogen detection	\$ 8,000,000.00	\$ 8,000,000.00
	2. Develop and test methods to improve the understanding of risk including how human behavior contributes to the risk of disease emergence	\$ 7,000,000.00	\$ 7,000,000.00
	3. Grand Challenges for Development: Fighting Ebola	\$ 8,974,686.00	\$ -
	4. Grand Challenges for Development: Combating Zika and Future Threats	\$ 30,000,000.00	\$ -
	Total	\$ 53,974,686.00	\$ 15,000,000.00

HIV and AIDS	1. Strengthen the programmatic evidence base for HIV/AIDS prevention, care and treatment to achieve epidemic control	\$ 3,843,750.00	\$ 4,732,557.00
	2. Accelerate development and clinical testing of novel HIV vaccine candidates and strengthen global capacity for vaccine research	\$ 28,710,000.00	\$ 28,710,000.00
	3. Develop, test and introduce microbicides for women to reduce the risk of HIV infection	\$ 45,000,000.00	\$ 45,000,000.00
	4. Improving HIV treatment through antiretroviral optimization	\$ 6,500,000.00	\$ 6,500,000.00
	Total	\$ 84,053,750.00	\$ 84,942,557.00
Family Planning & Reproductive Health	1. Refine, develop, and introduce new contraceptive methods	\$ 9,747,925.00	\$ 12,758,539.00
	2. Improve and expand access to family planning methods in developing countries	\$ 14,309,000.00	\$ 15,358,042.00
	3. Develop and introduce effective, scalable service delivery models to increase the healthy timing and spacing of pregnancies	\$ 979,000.00	\$ 1,511,000.00
	Total	\$ 25,035,925.00	\$ 29,627,581.00
Maternal, Child, & Newborn Health	1. Improve the access and utilization of evidence-based approaches for quality maternal neonatal and child health	\$ 11,160,796.00	\$ 10,224,231.00
	2. Develop measurement and decision-making tools for maternal, newborn and child mortality and morbidity	\$ 1,284,550.00	\$ 4,026,396.00
	3. Build capacity for implementation research to improve program efficiencies, effectiveness and quality	\$ 993,341.00	\$ 2,320,279.00
	Total	\$ 13,438,687.00	\$ 16,570,906.00
Nutrition	1. Strengthen and expand the evidence base on integrated multi-sectoral approaches to improve nutrition outcomes, including reducing child stunting, maternal and child anemia, and micronutrient deficiencies	\$ 1,713,051.00	\$ 123,634.00
	2. Support implementation research for improved dietary diversity and quality	\$ 1,130,789.00	\$ 1,781,115.00
	3. Develop, refine, and expand use of state-of-the-art measurement tools for nutrition programs and policies	\$ 209,379.00	\$ 253,660.00
	Total	\$ 3,053,219.00	\$ 2,158,409.00
Health Systems Strengthening	1. Research to measure progress and trace health impacts of health systems strengthening (HSS) investments	\$ 667,867.00	\$ 1,179,792.00
	2. Research to identify effective interventions that integrate two or more HSS functions	\$ 1,712,402.00	\$ 933,124.00
	3. Evaluations of HHS interventions	\$ 261,237.00	\$ 111,300.00
	Total	\$ 2,641,506.00	\$ 2,224,216.00
Total Funding	\$ 209,191,841.00	\$ 181,179,475.00	

* Neglected and Tropical Disease activities in this report were supported with \$3,000,000 in multi-year FY 2014 funds obligated in FY 2015.

Appendix II: Interagency Agreement with HHS/CDC to Prevent, Detect, and Respond to Zika

In 2015, USAID and HHS/CDC signed an Interagency Agreement (IAA) to collaborate to prevent, detect, and respond to the transmission of Zika virus. HHS/CDC's efforts to combat Zika reflect its world-renowned expertise in disease-surveillance, laboratory-strengthening, the surveillance and control of mosquitoes, and related public health research.

The countries in which HHS/CDC conducts activities through this IAA are Barbados, Belize, Brazil, Colombia, Costa Rica, the Dominican Republic, El Salvador, Ecuador, Grenada, Guatemala, Guyana, Haïti, Honduras, India, Indonesia, Jamaica, Kenya, México, Nicaragua, Panamá, Paraguay, Perú, Sierra Leone, South Africa, Thailand, Trinidad and Tobago, Uganda, and Uruguay. In addition, HHS/CDC works through this IAA with regional bodies that representing Member States such as the Caribbean Public Health Agency (CARPHA); the Caribbean Community (CARICOM); and the Pan American Health Organization (PAHO), which is the regional office of the WHO in the Americas.

This two-year IAA concluded intramural activities on September 30, 2017; extramural activities will finish by May 31, 2018, and close-out activities by December 31, 2018. The IAA contains 25 statements of work funded by USAID, categorized into six functional areas:

Management and Coordination of Emergency Response

HHS/CDC engages partners to enhance the management and coordination skills of public health officials in affected countries to respond to Zika through improved staffing and technical assistance and training for risk-assessment and communication.

Management and Control of Mosquitoes

HHS/CDC provides technical assistance to partners to conduct surveillance of mosquitoes and monitor the development of their resistance to insecticides; plan and manage integrated mosquito-control strategies (including the selection of applications and active ingredients and resistance-mitigation); and design, implement, and interpret evaluations to determine the public health impact of mosquito-control programs.

Innovations

HHS/CDC provides technical assistance for field studies, and develops plans for rolling out, and evaluating, new diagnostic tools for reference labs and potential private-sector partners, while focusing on differentiating Zika from chikungunya and dengue.

Laboratory Capacity, Accelerated Diagnosis, and Equipment

HHS/CDC is training laboratory personnel on molecular, serologic, and pathological diagnostics for Zika; developing and evaluating new diagnostic platforms; and supporting the production and global distribution of key Zika diagnostic reagents for surveillance purposes.

Interventions in Maternal and Child Health and Other Service-Delivery

HHS/CDC provides technical assistance to address the management of severe disease manifestations (*e.g.*, Guillain-Barré Syndrome) that affect reproductive-age women and children (the USAID target group), as well as other populations.

Surveillance, Epidemiology, and Public Health Studies

HHS/CDC supports surveillance and epidemiologic studies to document the prevalence of, and risk factors for, severe health outcomes related to Zika. The focus is on laboratory-based surveillance to confirm infection, surveillance systems for birth defects and severe neurologic disease, and epidemiologic studies to identify risks.

Major activities supported through the IAA include the following:

- Proyecto VEZ (*Proyecto de Vigilancia de Embarazadas con Zika*) conducts enhanced surveillance of pregnant women with Zika virus infection in three cities in Colombia. The study enrolled over 1,200 pregnant women with symptomatic Zika virus disease, and will follow their infants through their second year of life to document any adverse physical and neurodevelopmental outcomes.
- *Zika en Embarazadas y Niños (ZEN)* is a prospective cohort study of pregnant women, their infants, and their partners in selected sites in Colombia. Researchers follow pregnant women in their first trimester and their partners through delivery or the end of pregnancy, and their live-born infants through six months of age. The study involves the collection of biologic samples, clinical data and self-reported information on risk factors, and the tracking of growth and developmental outcomes among the infants. The study will identify incident Zika infection in pregnant women and their partners, and detect persistent viremia.
- The Zika Outcomes and Development of Infants and Children (ZODIAC) study in Brazil includes children from 12 to 24 months of age with evidence of congenital Zika virus infection, with and without microcephaly, and their caregivers. It collects information on the range of long-term health and developmental outcomes associated with congenital infection among children, the association between poor outcomes, the repercussions of congenital infection on the functioning of families, and their care needs.
- HHS/CDC has supported active surveillance for Zika and laboratory testing for Zika virus infection in cohorts of pregnant women in several countries, including Panamá, El Salvador, Haïti, and Indonesia. HHS/CDC also provides technical assistance to the Colombian Ministry of Health in its full investigation of all reported cases of microcephaly, other serious brain anomalies, and other major birth defects potentially associated with congenital Zika virus infection, to clarify the relationship between infection during pregnancy and severe fetal and infant outcomes.
- HHS/CDC piloted a new type of survey in Brazil and the Dominican Republic, administered through mobile devices, that enables mixed-method evaluation or research to take place in parallel by coupling closed-ended items with an option to add pictures, video, and voice recordings to an answer by a respondent.
- HHS/CDC established human-animal interface and vector surveillance in Zika virus-prone transmission areas to obtain pertinent epidemiological and ecological information needed to understand the dynamics of the introduction of the virus and identify factors that could be involved in its potential zoonotic circulation in Brazil, Colombia and Perú. HHS/CDC added entomological monitoring to a longitudinal cohort study in Thailand to assess the entomological risk associated with Zika transmission, and the efficacy of an intensified vector-control intervention on preventing Zika infection in pregnant women in Thailand.

These studies are providing valuable information that has informed the public health response to Zika, both abroad and in the United States. They are helping to improve diagnosis of the virus; prevent new infections; and fill critical knowledge gaps on the associations between Zika virus infection, neurologic manifestations and fetal and early childhood outcomes.

IAA Research Expenditures

The HHS/CDC research activities described in this appendix have received FY 2015 funding from USAID. The amount of these funds expended by HHS/CDC for research to date is \$10,577,490.