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**U.S. Agency for International Development
Report to Congress
on Health-Related Research and Development for Fiscal Year 2019**

The U.S. Agency for International Development (USAID) submits this report pursuant to Section 7019(e) of Division G of Public Law 116-94, the Department of State, Foreign Operations, and Related Programs Appropriations Act, 2020, which incorporates by reference the requirements of House Report 116-78 and Senate Report 116-126.

Senate Report 116-126: Not later than 60 days after enactment of the act, the USAID Administrator shall submit the annual report to the appropriate congressional committees on USAID's health-related research and development strategy, which shall include: (1) specific health product development goals, including timelines for product development; (2) details about ongoing and planned investments in drugs, vaccines, diagnostics, and devices, including collaboration with other Federal agencies as well as private sector partners; (3) a detailed description of the mechanisms for collaboration and coordination in support of global health product development between Federal agencies; (4) an assessment of any critical gaps in product development for global health; and (5) recommendations for filling such gaps to ensure that U.S. investments in global health research are efficient, coordinated, and effective.

USAID funds research and development (R&D) in global health that focuses on advancing new technologies and innovative approaches to increase efficiencies, address critical unmet needs, and improve the impact of health programs. Priority updates from Fiscal Year (FY) 2019 in these two areas appear below.

I. Research and Development into Health Products

Tuberculosis (TB): USAID continues to prioritize the development of effective, shorter treatment regimens for drug-resistant TB, including the evaluation of a new treatment regimen for extensively drug-resistant (XDR) TB that contains a novel combination of three drugs: pretomanid, linezolid, and bedaquiline. In FY 2019, the U.S. Food and Drug Administration (FDA) within the U.S. Department of Health and Human Services (HHS) approved the use of the regimen based, in part, on data from the USAID-funded study. USAID continues to fund the evaluation of other TB-treatment combinations that contain pretomanid. Further, the Agency is funding an open-label Phase III clinical trial to evaluate the efficacy and safety of a combination regimen of bedaquiline, delamanid, linezolid, and clofazimine in patients with multidrug-resistant (MDR) TB in the Republic of South Africa. USAID is also evaluating the efficacy of the same regimen in an open-label Phase III

observational clinical trial for patients with pre-XDR TB and XDR TB in the Republic of India. USAID has completed a randomized clinical trial that compares the effectiveness of a single round of isoniazid and rifapentine (3HP), given once a week for three months, versus two annual rounds of 3HP, in people who are living with HIV in multiple countries. This data will inform future policies and guide programs on best options for TB preventive therapy.

Global Health Security: USAID funds the collection of surveillance data on zoonotic pathogens (those able to infect both animals and people) that circulate in wildlife, livestock, and human populations. Data feed into a publicly available global database that allows for the identification of high-risk settings that might be associated with outbreaks, especially of novel organisms. Since 2014, USAID's investments have resulted in samples collected from more than 93,000 animals and 16,000 people in 28 countries and the discovery of 990 novel viruses. In West Africa, which suffered a crippling epidemic of Ebola beginning in 2014, USAID's funding enabled the Agency's partners to detect the Marburg virus in bats, which was not previously known to be present in the region, and a new species of Ebola virus (Bombali); both findings allow surveillance teams, laboratories, and health care facilities to update their protocols to include these threats. In the Democratic Republic of Congo (DRC) and the Republic of Uganda, studies have identified evidence of previously unrecognized Ebola exposure in humans. USAID's partners have produced high-resolution maps that identify the areas of highest risk for the emergence of new diseases, as well as more than 110 peer-reviewed publications regarding the spillover, amplification, and spread of zoonotic diseases. Surveillance data in Asia on influenza viruses that circulate among farm animals continue to shed light on the distribution, diversity, seasonality, and evolution of this virus family. USAID also funded the development and validation of an easy-to-use field test for H7N9 avian influenza; the test can produce results in two hours by non-experts and potentially is adaptable to other pathogens.

Neglected Tropical Diseases (NTDs): USAID previously reported on the development, field-testing, and policy change for a remapping protocol to identify non-endemic regions for lymphatic filariasis, which reduced unnecessary treatments and saved tens of millions of dollars. As of FY 2019, six additional governments have implemented the remapping tool. Since the World Health Organization (WHO) has endorsed the tool, tens of millions of people globally will avoid unnecessary treatment. USAID is continuing to fund a multi-country trial that tests the efficacy of a six-week course of doxycycline to improve the clinical outcomes and quality of life of patients with filarial lymphedema (sometimes called elephantiasis). Results from this study could redefine global strategies for the treatment of patients with moderate disease, which would reduce morbidity and improve quality of life. USAID is also establishing a catalytic fund for diagnostics for NTDs to improve monitoring and evaluation.

Malaria: USAID's Malaria Vaccine Development Program (MVDP) financed several research activities to develop novel or improved candidates for vaccines against malaria. Specifically, the MVDP completed a clinical trial of a multi-antigen vaccine that targets the liver stage of the parasite's life cycle, and initiated work on a vaccine trial that targets the infectious stage of its life cycle. Additionally, the MVDP funded several pre-clinical research studies to evaluate malaria antigens and vaccine-delivery platforms to inform the

design of novel or improved malaria-vaccine candidates. USAID continued to finance the development of antimalarial drugs through the Medicines for Malaria Venture, including research toward novel antimalarials to address drug-resistance and create child-friendly formulations of existing drugs. USAID funds the development of critical new insecticides for bed nets and indoor residual spraying (IRS) through the Innovative Vector-Control Consortium. These new insecticides are urgently needed to address the growing resistance to existing insecticides that is spreading throughout sub-Saharan Africa. In addition to funding the development of nearly a dozen promising novel insecticides for enhanced control of mosquitoes, USAID also funds the development of novel technology for the application of IRS to improve the coverage of insecticides, reduce waste, and maximize efficiency.

HIV/AIDS: Under the President's Emergency Plan for AIDS Relief (PEPFAR), USAID is funding regulatory approval and introduction of the 30-day dapivirine ring, the first non-systemic microbicide for the prevention of HIV in women that multiple, randomized clinical trials have shown to be safe and effective. USAID is also investing in other long-acting microbicides, including biodegradable implants; dermal patches; broadly neutralizing, antibody-based, long-acting injectables; and a 90-day, multi-purpose dapivirine ring. Activities to introduce the dapivirine ring and scale up oral pre-exposure prophylaxis are under way, essential to ensuring access to these products for the women who need them. In addition, USAID funds the International AIDS Vaccine Initiative to conduct epidemiological studies, characterize the immune response to HIV in African populations, and strengthen capacity at African clinical-research sites that serve as go-to centers for vaccine trials.

Voluntary Family Planning/Reproductive Health: For decades, USAID has been a leading funder of new fertility-awareness methods (FAM). USAID financed the first clinical trial of a contraceptive mobile-phone application (app) and, in FY 2019, results showed that the app is as effective as user-controlled hormonal contraceptive methods. USAID's investments in FAM highlight an area in which partners now will integrate the findings of successful biomedical research routinely into planned service-delivery projects. USAID is also one of several donors that financed the Evidence for Contraceptive Options and HIV Outcomes Study, which evaluated whether three widely used contraceptives influence the risk of acquiring HIV. Announced in June 2019, the results of the study showed no significant difference in the risk of HIV acquisition among the three methods, and the WHO revised its guidance regarding the use of contraception by women at high risk of acquiring HIV. The revised guidance does not recommend restricting contraceptive choice on the basis of the risk of acquiring HIV.

Maternal and Child Health (MCH): Through the Saving Lives at Birth (SL@B) partnership, USAID funds the scale-up of promising technologies, including the Universal Anesthesia Machine (UAM), a workstation that can function without power or compressed oxygen. USAID funds the provision of the UAM, along with skills-training and customer service, to equip providers with low-cost, safe anesthesia for surgeries in emergency settings. USAID also provides funding for the NEST360° bundle, a private-public partnership to scale sustainably a package of 17 technologies that address the major causes of newborn death in Africa. NEST360° will work with local professional schools to train new innovators and private foundations to leverage more than \$68 million.

II. Implementation Science Research

TB: USAID continues to fund studies that combine whole-genome sequencing data with spatial, epidemiological, demographic, and laboratory information to understand and prevent the transmission of MDR TB.

Global Health Security: USAID funds in-depth research to locate high-risk populations, social preferences, and practices linked to risky contact between humans and animals. This information provides an understanding of interventions to reduce the risk of spillover. Following the discovery of the Ebola Bombali strain in bats, which roost in houses in West Africa, USAID-funded partners have developed educational tools now deployed to at-risk communities. Bats play an essential role in controlling mosquito populations, so these tools are important to provide information on how to reduce the risk of both bat- and animal-borne diseases. Researchers are now using the findings to develop and test interventions to reduce the spillover risk of zoonotic pathogens, such as Ebola, Nipah, influenzas, and coronaviruses.

Malaria: Through the President's Malaria Initiative (PMI), USAID financed operational-research activities to improve the delivery of malaria-control interventions. Studies completed in FY 2019 included a feasibility study of the community delivery of preventive malaria treatment for pregnant women in Burkina Faso and an evaluation of novel IRS techniques in the Republic of Ghana to improve the cost-effectiveness of this critical intervention. Ongoing studies included research to reduce transmission in priority regions, methods to improve care-seeking behavior for febrile illness, and research on the feasibility and effectiveness of extending community case-management to all age groups. Additionally, USAID, through PMI, collaborated with Unitaid and the New Nets Project funded by the Global Fund to Fight AIDS, Tuberculosis, and Malaria to build evidence on the public-health impact and cost-effectiveness of insecticidal bed nets treated with new insecticide combinations throughout sub-Saharan Africa. These new tools are critical to combating resistance to insecticide, which is one of the greatest challenges to eliminating malaria.

Maternal and Child Health: USAID is accelerating South-to-South learning to improve the quality of care and survival of mothers and children. Partners in the Republics of Madagascar and Malawi are evaluating innovative approaches to the timely identification, referral, and treatment of postpartum hemorrhage, a major global killer of women. This work complements ongoing research in Ghana and Uganda to improve care-seeking and emergency referral systems for mothers and their babies. Additionally, USAID used co-design with key stakeholders to launch implementation research in Kenya to define challenges within maternal and child health in urban slum settings, a potential obstacle on the Journey to Self-Reliance.

Voluntary Family Planning/Reproductive Health: USAID funds innovative approaches to reaching adolescents with appropriate information on fertility awareness and protective behaviors. In September 2019, a USAID partner launched an eight-week pilot program to test its digital platform, which aims to improve the health and livelihoods of urban adolescents in Rwanda. Data generated from this pilot will inform a large-scale, randomized control trial in more than 60 schools across eight Districts, which is

scheduled to begin in April 2020.

HIV/AIDS: Through PEPFAR, USAID invests in implementation science and operations research to generate timely evidence to fill local gaps in data and address critical operational challenges for scaling-up antiretroviral therapy; leveraging community platforms more effectively; strengthening the continuum of care; and reducing social and structural barriers to prevention, treatment, and care. USAID's implementation-science investments help to achieve the "95-95-95" goals set by the Joint United Nations Programme on HIV/AIDS, while contributing to PEPFAR's commitment to investing in evidence-based interventions within targeted geographic areas and populations to maximize impact and achieve control of the epidemic more rapidly.

Nutrition: USAID funded an implementation-science study in the Republic of Mozambique to identify and remove barriers to exclusive breastfeeding. The Agency funded partners to conduct research on the revitalization and scale-up of the Baby-Friendly Hospital Initiative in Malawi, the rollout of integrated nutrition and voluntary family planning programming in the United Republic of Tanzania, the strengthening of nutrition services within integrated community case-management (iCCM) in the DRC, governmental actions for accelerating progress for complementary feeding in Kenya, and the global implementation of the Baby-Friendly Community Initiative. Moreover, USAID funded research to assess the quality of anthropometric data in Demographic and Health Surveys and examine coverage and the role of health facilities in adherence to iron and folic-acid supplementation during pregnancy and support for early breastfeeding. USAID also funded studies to reduce iodine-deficiency disorders, such as research on the effects of excess iodine intakes in East Africa, the health and economic benefits of universal salt iodization, and the effectiveness of double-fortified salt programs. This research is helping building capacity, changing policies, and creating and enforcing regulation frameworks to strengthen the production, distribution, and consumption of high-quality iodized salt to prevent iodine-deficiency disorders.

Health Systems: USAID completed a landscape analysis to identify evidence-based enhancements to supervision approaches that demonstrate significant improvements in the performance of health workers, the quality of health care, and the effectiveness of health institutions. Key findings from this analysis showed that the supervision of health workers is most effective when adapted to specific contexts that address identified performance challenges at the macro-, micro-, and individual level. USAID funded the development of a white paper to examine the financial costs of substandard and falsified medicines and their implications for access to Universal Health Care (UHC). This report demonstrates the benefit of ensuring the quality of medicine in expanding access to UHC, explores the association between access to UHC and the quality of medicine in the context of essential medicines in low- and middle-income countries, assesses the health and economic impact of poor-quality antimalarials in a case study, and provides recommendations to integrate quality-assurance for medicines into programming to offer access to UHC.

Appendix I. The Approach of the U.S. Agency for International Development to the Product-Development Process

The process of developing new global health technologies, and delivering them to those who need them most, requires considerable time and resources. Often the resources required to develop and implement a product cannot come from one donor; rather they demand resources and effort from a diverse array of partners. Each of the program areas in global health of the U.S. Agency for International Development (USAID), in consultation with Congress, establishes priorities for investment and works with the global donor community to set goals, identify gaps, align agendas, share knowledge, and coordinate funding. This highly dynamic landscape requires effective and constant communication, as well as the flexibility of resources to respond to rapid changes in the field. For example, while considerable funding might be required in one year to support a large efficacy trial of a product, financial resources are also critical in subsequent years to ensure the effective implementation and introduction of the product within programs, especially in USAID's priority countries.

USAID's goals in research and development in global health, as well as our approach to the R&D process, appear broadly outlined in the Agency's *Global Health R&D Strategy (2017–2022)*. Across USAID's R&D portfolio, critical gaps and needs in the field constantly evolve. Central to the Agency's approach is regular consultation and coordination with other donors, including international organizations, private-sector entities, and other U.S. Government Departments and Agencies. In our *Report to Congress on Health-Related R&D for Fiscal Year (FY) 2018*, USAID outlined key examples of our efforts to coordinate with other donors. Since the submission of the FY 2018 report, USAID has worked to advance this collaboration. Notably, as part of a new Memorandum of Understanding (MOU) between USAID and the National Institutes of Health (NIH) within the U.S. Department of Health and Human Services (HHS), the two organizations held their first annual meeting to share priorities in global health research and identify several areas for potential enhanced collaborations. One follow-up action is a plan for USAID to join a growing group of organizations that voluntarily post information about biomedical research investments on the HHS/NIH-funded World Report database. Sharing information more publicly about the Agency's investments is important for transparency and for the global health community to identify areas of potential collaboration and learning.