U.S. Agency for International Development
Report to Congress
on Health-Related Research and Development (R&D) for Fiscal Year 2020

The U.S. Agency for International Development (USAID) submits this report pursuant to Section 7019(e) of Division K of Public Law 116-260, the Department of State, Foreign Operations, and Related Programs Appropriations Act, 2021, which incorporates by reference the requirements of House Report 116-444 and the FY 2021 Joint Explanatory Statement (JES).

House Report 116-444: The Committee directs the USAID Administrator to continue the annual report on health-related research, which is important for transparency and oversight of the agency's work on global health research to be submitted not later than 45 days after enactment of this Act and posted on a public website.

FY 2021 JES (incorporated by Sec. 7019(e) of PL 116-260): Not later than 60 days after enactment of the act, the USAID Administrator shall update the report required under this heading in Senate Report 116–126 on USAID's health-related research and development strategy in the manner described.

Senate Report 116-126: Research and Development. The Committee recognizes USAID's role in health-related research and supports continued investments in new global health technologies across each of USAID's health-related programs to address longstanding and emerging global health challenges. 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's *Global Health R&D Strategy (2017– 2022)* broadly outlines the Agency's Global Health R&D goals and its approach to the R&D process. USAID, in consultation with Congress, establishes priorities for investment working alongside the global community, including partner countries, non-profit and multilateral organizations, private sector partners, and other U.S. Government partners. Collaboration among these partners ranges from informal data sharing and coordination of investments, to more formal agreements like co-funding activities or leveraging infrastructure established through other partner investments. In the coming months, USAID will begin developing its Global Health Research Strategy beyond 2022, which will include consultations with key partners like those previously outlined. USAID will use this opportunity to reevaluate its approach to Global Health R&D, including how it works with other U.S. Government partners and the international community, to fill gaps and achieve goals in a rapidly changing global health landscape. The report below outlines key developments and collaborations since the FY 2019

report and highlights new areas of investment for the coming fiscal year.

I. Research and Development into Health Products

Tuberculosis (TB): The development of effective, shorter, and well-tolerated treatment regimens remains a major priority. USAID continues to evaluate the efficacy and safety of new treatment regimens that contain new TB medicines, including: Pretomanid, Bedaquiline, and Delamanid, for multidrug-resistant (MDR) TB and extensively drug-resistant (XDR) TB. After an interruption due to COVID-19, enrollment has resumed for USAID-supported Phase III clinical trials evaluating combinations of Bedaquiline, Delamanid, Linezolid, and Clofazimine for the treatment of XDR TB in India and MDR TB in South Africa. These studies are recording incidence of COVID-19 among study participants, with the goals of evaluating the impact of COVID-19 on study outcomes, as well as performing a real-time assessment and analyses of lessons learned from conducting clinical trials during a pandemic.

Global Health Security: USAID partners published more than 160 journal articles, books/chapters, studies, and other publications related to the spillover, amplification, and spread of zoonotic diseases and antimicrobial resistance — information critical to preventing and responding to future infectious disease outbreaks. USAID worked to identify the animal source of the SARS-CoV-2 virus, which has caused the COVID-19 pandemic, through screening its archives of animal and human samples from Asia (collected from 2009 to 2020) for evidence of active or previous infections with the pandemic virus and/or related coronaviruses. From 3,631 animals prioritized for testing, SARS-related coronaviruses were detected in specimens from nine bats and pangolins and non-SARS-related coronaviruses were detected in specimens from 72 additional bats. As part of these efforts, a journal article reporting on work funded by USAID demonstrated that bats that lived in a Cambodian cave in 2010 carried a virus that shared 92.6 percent similarity to SARS-CoV-2. In order to implement measures that protect human populations from future spillovers, this information can be used to both narrow the search for animals that carry the SARS-CoV-2 virus and understand how these animals come into contact with people.

Neglected Tropical Diseases (NTDs): USAID is supporting the new World Health Organization Diagnostics Technical Advisory Group (WHO DTAG) for NTDs, to establish new Target Product Profiles (TPPs) for preventive chemotherapeutic NTD diagnostics, notably for Lymphatic Filariasis and Onchocerciasis, to diversify the products on the market and improve field performance. A request for proposals addressing laboratory and field performance evaluations, through the U.S. Centers for Disease Control and Prevention (CDC) within the U.S. Department of Health and Human Services (HHS), will guide final selection and recommendation for uptake in national elimination programs for surveillance of both diseases. Additionally, USAID is continuing to fund a multi-country trial to evaluate the efficacy of a six-week course of doxycycline to improve the clinical outcomes and quality of life of patients with Lymphatic Filariasis (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.

Malaria: USAID's Malaria Vaccine Development Program (MVDP) made investments in several research activities to develop novel or improved candidates for vaccines against malaria. Specifically, the MVDP completed a first-in-human clinical study of a vaccine that targets the infectious stage of the malaria parasite 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 to stop infection or disease caused by the parasite. 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 continued to fund 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 continues to support the development of and regulatory procedures for the 30-day dapivirine ring ("the ring") and introduction efforts for both the ring and long-acting cabotegravir (CAB-LA). The ring received a positive scientific opinion from the European Medicines Agency in July 2020 and received World Health Organization (WHO) pre-qualification in November 2020, confirming that it meets global standards for quality, safety, and efficacy. CAB-LA, a bi-monthly injectable antiretroviral (ARV), has shown significant protection in clinical trials, and alternative CAB-based formulations are planned for clinical testing. USAID is also investing in other novel agents and delivery systems at earlier stages of research, including biodegradable implants; dermal patches; broadly neutralizing antibody-based, long-acting injectables; and a 90-day, multi-purpose dapivirine ring. Activities to introduce the ring and CAB-LA and further scale up of oral pre-exposure prophylaxis are underway to ensure that women, especially adolescent girls and young women, have access to an optimal selection of HIV prevention products that are safe, effective, acceptable, and affordable. In addition, USAID funds the International AIDS Vaccine Initiative (IAVI) to develop and test candidate HIV vaccines, conduct epidemiological studies, characterize immune responses to HIV in African populations, and strengthen capacity at African clinical-research sites that serve as go-to centers for clinical trials of candidate vaccines and other novel biomedical prevention products.

Voluntary Family Planning/Reproductive Health: USAID continues to support the development of a microneedle patch, offering women an innovative, discreet, longer-acting contraceptive with simple, safe self-administration without generating biohazardous sharps waste. Sustained release for more than one month was achieved and work is ongoing to achieve longer duration targets. 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. Based on study outcomes, WHO revised its guidance to recommend not restricting contraceptive choice based on risk of acquiring HIV. The updated recommendations were disseminated worldwide, and these efforts enabled governments and key stakeholders to learn, understand, and implement the new recommendations in their work.

Open Innovation: USAID supports a broad range of global health innovators engaged in R&D by running Grand Challenges, cultivating innovation communities, and supporting innovators as they scale. These initiatives harness the power of crowdsourcing, competition, and partnerships to identify breakthrough innovations around critical health and development problems. For instance, through the Saving Lives at Birth (SL@B) partnership, USAID has supported several of the innovations forming the NEST360° bundle, a private-public partnership to scale a package of 17 technologies that address the major causes of newborn death in Africa. Leveraging more than $68 million in new external funding, NEST360° will work with local professional schools to scale and maintain the package of innovations as well as to train new innovators.

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. The sequencing of the Mycobacterium TB genome was temporarily interrupted as laboratories performing genome sequencing shifted focus to COVID-19.

Global Health Security: As part of its Global Health Security research efforts, USAID promoted

the research capacity of partner country universities by providing small grants to faculty and students to conduct applied research on a wide range of "One Health" topics — 10 of which have been published in peer-reviewed publications. USAID partners also conducted research to assess laboratory capacity in partner countries; conducted surveillance and mapping of various zoonotic diseases including avian influenza, swine influenza, MERS-CoV, SARS-CoV-2, and Nipah virus in different countries and regions; carried out situational analyses of various regional workforce development programs in Asia and Africa; documented best practices for risk management and reduction measures for various zoonotic diseases; and conducted impact assessments of various zoonotic disease outbreaks, including COVID-19. Finally, as a leader in antimicrobial resistance stewardship, multisectoral collaboration and infection prevention and control, USAID published two research papers on antimicrobial stewardship and worked in collaboration with the WHO to develop an Access to Medicines Global Benchmarking Tool.

Malaria: Through the President's Malaria Initiative (PMI), USAID supported operational research activities to optimize the delivery of malaria-control interventions, evaluate the expansion of access to malaria prevention and treatment services, and assess new and effective tools against malaria. Studies completed in FY 2020 included an evaluation of the impact of extending seasonal malaria chemoprevention from the standard age group (3-59 months) to older children (5-10 years) in Mali, an assessment of the effectiveness of intermittent screening and treatment of malaria in pregnancy on maternal and birth outcomes in Rwanda, and an evaluation of a highly sensitive rapid diagnostic test for malaria detection in low transmission areas in the Kingdom of Cambodia. Ongoing studies included research focused on new and effective tools to reduce malaria in low to moderate transmission areas, the feasibility and effectiveness of extending community case-management to all age groups, and novel approaches to improve the delivery of proven malaria control interventions such as IRS. 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, one of the greatest challenges to eliminating malaria.

Maternal and Child Health: USAID is accelerating learning to improve both quality of care and survival of mothers and children. The USAID-WHO 52-country study on the intrahospital management of maternal infection complications revealed an even greater role for early identification and prompt evidence-based management of infections in reducing maternal deaths in USAID-supported countries. Following a recent USAID-supported trial in sub-Saharan Africa that provided new understanding of the normal progress of labor, WHO developed a guide as an alternative to the "partograph" that has been used for decades to assess the progress of labor. The USAID-completed study in Burma expands the evidence on the experience of women in childbirth facilities with the first use of gender analysis to explore how gender dynamics and power relations contribute to women's experiences of mistreatment. This evidence provides the basis for dialogue between mothers and caregivers to understand and eliminate patterns of abuse in childbirth that have become normalized. Early research results in Kenya show a two-way communication system with critical health messages, personalized advice, and referrals for urgent medical needs increased utilization by women in informal urban settlements. Additionally, even with broad use of evidence-based guidelines like child illness case management, a multi-country USAID study shows that there are still many adherence gaps impacting quality of child case management -- especially in checking for danger signs, severe disease, and acute malnutrition. Uptake of the research findings will help improve programs in many USAID-supported countries where the burden of child mortality is high and where the private sector is an important source of sick child care. Additional research in Kenya shows how to implement, monitor, and evaluate a set of family-centered interventions for newborns and sick children in hospital settings; identify the short-term health outcomes for mothers, newborn, and children; and generate lessons for replication at scale. The

study includes aspects of nurturing care with emphasis on how to improve provider-parent partnership, mutual trust, how to cope with difficult environments and provide emotional support and coaching to parents. Finally, USAID research identified the verbal and social autopsy to be an important tool for understanding child mortality drivers and identifying potential solutions for a range of stakeholders. Research uptake was facilitated by early and ongoing stakeholder engagement, a key component of implementation research.

Voluntary Family Planning/Reproductive Health: In response to early concerns around COVID-19 disrupting family planning programs, USAID responded to the global need for guidance and data by supporting the development and implementation of qualitative research intended to rapidly collect and disseminate data on the impact of COVID-19. To date, 14 countries have requested to use the questions in ongoing programs and studies. Generating standardized information will improve the understanding of the pandemic's impact on family planning access and use and will support program adjustments and generate broader learnings to inform the response to future epidemics and pandemics.

NTDs: For the third year, the African Research Network for Neglected Tropical Diseases (ARNTD), with support from USAID and UK Aid, provided small grants to address operational and implementation research on ''Emerging Challenges facing NTD program implementation in Africa.'' This year, the grant was awarded to 12 African researchers in both early and mid/late career to undertake operational or implementation research aligned with the goals established in the London Declaration on Neglected Tropical Diseases.

HIV/AIDS: Through PEPFAR, USAID has invested in implementation science and operations research to generate timely evidence to fill local gaps in data and address critical operational challenges for scaling-up ARV therapy; leveraged community platforms more effectively; strengthened the continuum of care; and reduced 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: Beginning in 2021, USAID will support two implementation research studies intended to improve infant and young child feeding counseling. The studies aim to improve skilled lactation counseling training for health providers, as well as community health worker counseling skills on nutrition and pneumonia. USAID also seeks to understand causes and current global prevalence and severity of micronutrient deficiencies, with special emphasis on iodine deficiency disorders and anemia. Indicators to assess iodine adequacy in children and women were studied in countries with distinct climatic conditions. USAID supported improved methodologies for reliable determination of hemoglobin concentration and the influence of pregnancy and high-altitude, which will inform new WHO recommendations. As part of the Demographic and Health Survey (DHS) Program's continuous efforts to collect and disseminate high-quality data, the program developed a composite anthropometry data quality index to rank the quality between surveys and performed simulation models to assess the impact of measurement error on anthropometric estimates. Efforts were initiated for the appropriate use and interpretation of child stunting data, as well as the promotion of complementary indicators suitable to assess quality of nutritional interventions, among them development of practical methodologies to determine quality and adequacy of diets.

Health Systems: USAID conducted health systems strengthening (HSS) research and published HSS evidence across multiple topics. In Guinea, USAID conducted a landscaping analysis and collaborated with Ministry of Health officials to select three implementation research questions which USAID will support to advance and ensure successful implementation of the National Community Health Strategy. The results will inform community health strategy implementation

globally. In Ghana, USAID is supporting implementation research to understand the impacts of the government's Primary Care Provider (PCP) Network initiative. Findings will examine how PCP networks promote Ghana's equity objectives for Universal Health Coverage and will contribute to global knowledge on equity-enhancing strategies. USAID also finalized and released a global guide for institutionalizing health technology assessments in low- and middle-income countries (LMICs), a rigorous policy process that enables transparent and systematic value-based decision making for product coverage and purchasing decisions. In addition to the antimicrobial stewardship papers noted previously, another was published on integrating pharmaceutical systems strengthening in global health programs, critical to supporting access to and appropriate use of life-saving medical products in LMIC health systems. Finally, USAID conducted a global landscape analysis and began country case studies on digital financial services (DFS) for health in order to establish an evidence base of emerging models of DFS for health and contribute guidance on why, how, and under what circumstances DFS investments contribute to achievement of health system outcomes.

Appendix I: Current Funding in Fiscal Year (FY) 2020 from the U.S. Agency for International Development for Health-Related Research and Development

	Applied Research	Development Research	Total
	FY 2020 Budgeted	FY 2020 Budgeted	FY 2020 Budgeted
HIV/AIDS		**73,710,000**	**73,710,000**
Tuberculosis (TB)	**9,133,332**	**15,150,970**	**24,284,302**
Malaria	**7,181,100**	**12,000,000**	**19,181,100**
Global Health Security in Development	**5,564,190**	**-**	**5,564,190**
Other Public-Health Threats	**5,011,120**	**-**	**5,011,120**
Maternal and Child Health	**7,459,285**	**1,042,645**	**8,501,930**
Voluntary Family Planning and Reproductive Health	**11,962,110**	**7,516,306**	**19,478,416**
Nutrition	**5,100,074**	**612,000**	**5,712,074**

Notes: The above table reflects the approved FY 2020 Operation Plan levels as of January 29, 2021. The HIV/AIDS funding for development research reflects the FY 2020 vaccines and microbicides Congressional directives. The table does not include HIV/AIDS research funding programmed through USAID Missions as part of Country Operational Plans for President's Emergency Plan for AIDS Relief.