Summary

In 2009 USAID launched the Emerging Pandemic Threats program (EPT-1) – a five year program targeting the early detection of new disease threats; enhanced “national-level” preparedness and response capacities for their effective control; and a reduction in the risk of disease emergence by minimizing those practices and behaviors that trigger the “spill-over, amplification, and spread1” of new pathogens from animal reservoirs to humans. EPT-1 complemented an ongoing line of work being supported by USAID since 2005 - to control the threat posed by highly pathogenic H5N1 avian influenza virus (AI).

Both of these efforts grew out of a recognition that we are now in an era of new, re-emerging and recurring global health threats that argue for a longer-term, more strategic approach to global health security. The EPT-1 and AI work have been focused on building those capacities and expanding the evidence base that contribute to mitigating the impact of novel “high-consequence pathogens” arising from animals. Using a “risk-based” formula that targeted those places, populations and practices that contribute to the spillover, amplification, and spread of new microbial threats, our EPT-1 and AI programs have laid the foundation for a next generation of investments that seeks to consolidate these efforts into a highly coordinated program to further minimize their potential for global impact.

Over the past several decades, many previously unknown human infectious diseases have emerged from animal reservoirs, including agents such as human immunodeficiency virus (HIV), SARS coronavirus, the highly pathogenic avian influenza H5N1, the 2009 H1N1 pandemic influenza virus and more recently the H7N9 influenza virus and the Middle East Respiratory Syndrome (MERS) coronavirus. In fact, more than three-quarters of all new, emerging, or re-emerging human diseases since the beginning of the 21st century have been caused by pathogens originating from animals or animal products. As the interactions between people and animals intensify, driven by increasing human populations, the spillover, amplification, and spread of new, deadly zoonotic disease threats will increase steadily in the coming decades.

Mindful of the looming challenge posed by emerging diseases, a long-term objective of the EPT-1 Program was an “experiment in action” – intended to answer the two-part question: is it possible to anticipate future pandemic threats before they emerge, and can their emergence be stopped? This introduction speaks to the significant advances made under USAID’s EPT-1 and

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1 “Spillover” is defined as an event in which a zoonotic virus is transferred from an animal host to humans. “Amplification” is defined as an increase in number of copies of a zoonotic virus, either in animal or human populations. “Spread” is defined as an increase in host range and/or geographic distribution of a zoonotic virus.
AI programs in describing the underlying drivers for viral spillover, amplification, and spread and the opportunities to build upon and extend their accomplishments over the coming five years under a consolidated EPT-2 program that unifies investments in influenza and other emerging viral threats under one strategic umbrella. Importantly, the expected progress to be achieved under EPT-2 will itself lay the foundation for future iterations of EPT and, hopefully, move towards a greater capability to "forecast" and stop" future threats before they fully emerge. This document also addresses how EPT-2 will contribute to the Global Health Security (GHS) Agenda - a White House led effort to consolidate US Government (USG) efforts across the health and security sectors to more effectively address threats posed by the natural spillover, amplification, and spread of new disease threats, as well as the intentional and/or accidental release of dangerous pathogens. Beyond consolidating USG efforts, the GHS agenda is also focused on creating a unified global effort to address these threats.

**Introduction: A Decade of Learning**

In today’s globalized world, the speed with which newly emergent diseases can surface and spread, as illustrated by the H1N1 2009 pandemic virus, raises serious public health, economic, security and development concerns. It also underscores the need for the global community to act pre-emptively and systematically to improve individual countries’ abilities to earlier identify and quickly mitigate health threats arising within their borders. Most importantly, the threat posed by new infectious diseases arising from animal reservoirs (zoonotic diseases) argues for a rethinking of standard strategies for the “prevention, detection and response” of diseases and their progenitors to reflect a more inclusive and strategic partnership across the public health, animal health and environmental sectors if we are to be able to address emergent disease threats before they pose an overwhelming global threat.

The emergence of the Severe Acute Respiratory Syndrome (SARS) coronavirus in 2003 and the H1N1-2009 pandemic influenza virus illustrate the consequences of not having in place capacities to detect the early stages of spillover, amplification, and spread of a new disease threat – that is, while it is still circulating (and evolving) principally in animals and before the potential threat has acquired the ability to efficiently transmit among humans. In both instances the public responses came after the viruses had fully emerged as pandemic threats. On the other hand, the emergence of the H5N1 highly pathogenic avian influenza virus in Hong Kong in 1997 and its re-emergence in Southeast Asia in 2003, and the early detection of H7N9 virus in China and the Middle Eastern Respiratory Syndrome (MERS) coronavirus in Saudi Arabia have provided important opportunities to monitor a threat after it has spilled over, but before large-scale amplification and spread – and enable the world a longer window to prepare for the possibility of a new health threat, including the production of diagnostics and vaccines and the stockpiling of antivirals. The early recognition of a potential threat also allows for a global
effort to take preemptive steps to bring the spread of the virus under greater control – and by extension possibly reduce the opportunities for it to emerge as a pandemic threat. Importantly, work, in part supported under USAID’s Global Health Security and Development Unit (GHSD) portfolio, has advanced our understanding of disease spillover, amplification, and spread by highlighting the strong correlation between “high risk” geographic areas, animal hosts, microbial agents, and people. This collective body of work, in turn, has led to the recognition that risk-based intervention strategies enable targeting disease detection to those places, populations, times or situations where risk of viral spillover, amplification, and spread is greatest and the likelihood of detecting these events is highest.

The “GHSD Portfolio”

USAID is a major leader in the global response to the dangers posed by emerging pandemic threats. Since 2005, the dual goal of USAID’s Global Health Security and Development (GHSD) program has been to: a) minimize the global impact of existing pandemic influenza threats, particularly from the H5N1 highly pathogenic avian flu, and b) pre-empt the spillover, amplification, and spread of future pandemic threats. The effectiveness of the three areas of focus by the GHSD program: 1. H5N1 Avian Influenza; 2. Pandemic Preparedness; and, 3. Emerging Pandemic Threats are described below.

1. H5N1 Avian Influenza: Since mid-2005, USAID, in partnership with the U.N. Food and Agricultural Organization (FAO), the World Health Organization (WHO), and national government and non-government counterparts, has strengthened the capacities of more than 50 countries for monitoring the spread of H5N1 avian influenza among wild bird populations, domestic poultry, and humans, to mount a rapid and effective containment of the virus when it is found, and to assist countries prepare operational capacities to mount a comprehensive response in the event that a pandemic-capable virus emerges.

USAID’s efforts have contributed to dramatic downturns in reported poultry outbreaks and human infections, and a dramatic reduction in the number of countries affected – as illustrated below.

(1) The overall magnitude of the H5N1 avian pandemic has diminished, with reported numbers of poultry outbreaks and human cases having decreased since their peak in 2006.

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Over the past several years there has been a substantial decrease in reported poultry outbreaks and human infections. Specifically, poultry outbreaks and human infections decreased about 64% between 2006 and 2013. The success in endemic countries has often been due to improvements in the efficacy of poultry vaccination; in epidemic countries success has been more closely linked to improvements in rapid detection and containment. Generally, behavior change communications has had limited impact as people have been reluctant to change the behaviors that put them at risk of infection when the “risk” of infection is recognized as a very rare event.

Indonesia is the most recent example of how the introduction of effective measures has led to a dramatic reduction in reported outbreaks in poultry and humans. In 2009 USAID initiated an effort with FAO and the OIE/FAO OFFLU Network for Animal Influenza to work with Indonesian authorities to develop and produce a poultry vaccine locally that specifically matched the H5N1 viral strain then circulating in Indonesia. In 2011 a highly effective vaccine was introduced and quickly taken up by the large scale poultry producers. By the end of 2012 there was a greater than a 60 percent reduction in reported H5N1 outbreaks among poultry and a similar reduction in reported human infections (see adjacent figure). Both reductions have been sustained through 2013. Importantly, as part of this activity the capacities for both monitoring for long-term efficacy of the vaccine against circulating H5N1 virus and the development of future poultry vaccines were institutionalized within Indonesia. USAID is now working to apply this model in Egypt, another persistent “hot spot” for H5N1.

(2) H5N1 appears to have not only stopped spreading to new countries, but there has also been a dramatic contraction of its geographic range.

H5N1 appears largely to have stopped spreading to new countries, at least for now. Between 2003 and mid-2005, nine countries in Southeast Asia reported H5N1 outbreaks. Beginning in late 2005, there was an explosive movement of the virus outside of Southeast Asia to Europe, the Middle East, South Asia, and Africa. At the height of the poultry outbreaks in 2006, a total of 53 countries had reported outbreaks. Between 2011 and 2013, the number of countries affected has been limited to 18, with five of these countries...
(Bangladesh, China, Egypt, Indonesia, and Vietnam) accounting for 91% and 71% of all reported poultry outbreaks and human infections, respectively.

(3) **Affected countries have strengthened their capacities to identify and respond to future poultry outbreaks.**

USAID has focused on strengthening the capacity of affected countries in three key areas: strengthening laboratories for the early identification of H5N1 infections in both poultry and people; promotion of timely and effective response in containment and elimination of the virus; and education of the general population on the risks associated with avian influenza and steps they can take to protect themselves. These investments have led to improved capacities in early-warning surveillance for AI outbreaks in domestic poultry, wild birds, and humans, have strengthened capacities of veterinary and human health laboratory diagnosis of the H5N1 virus, and have established rapid response teams involving veterinary and public health professionals trained in core principals of field epidemiology. All of these are key capacities that could form the backbone of any effort to address the larger threats posed by emerging zoonotic diseases.

Per the adjacent figure, a comparison of AI outbreaks by year indicates that the average number of days between the start of disease outbreak in poultry or wild birds and H5 or H5N1 confirmation has fallen from eight days (in 2006) to three days (in 2013). This is a strong indicator that the worldwide detection of AI outbreaks has dramatically improved which has contributed to the worldwide decrease in AI outbreaks in birds mentioned above.
Monitoring the spread of H5N1 and its genetic variants across Southeast Asia has led to an unexpected but important understanding of the role of commercial poultry “value chains” in the spillover, amplification, spread, and maintenance of influenza viruses. One consequence of improved laboratory capacities has been the ability to routinely monitor the spread of the H5N1 virus and its genetic variants (clades) across Southeast Asia. This has led to a growing appreciation of the role of commercial poultry trade – from farm to markets - in promoting the evolution of the virus, its spread across the region and its persistence in countries such as Vietnam and Indonesia. As a result, increasingly detailed “value chain” maps have been generated that describe the geographic routes by which poultry are moved from farms to markets, sometimes across thousands of miles. This has led to a better ability to anticipate how new viral variants might spread from the initial location where it first evolved. This knowledge has proven particularly useful in anticipating how the H7N9 virus, which emerged in eastern China in early 2013, might spread across China and into Southeast Asia. This information has also proven central to recent efforts to better understand the drivers behind the spillover, amplification, and spread of new influenza threats.

Although these successes against H5N1 are significant, as of 2014 the H5N1 virus remains a serious public health threat and sustained vigilance is required; the virus continues to spread in poultry with a mortality rate among infected humans of nearly 60% and has an undiminished capacity to re-spread across the world were existing control measures relaxed. As a reminder of the threat it poses, two new countries (North Korea and Libya) have recently reported the presence of the virus and over the past four years several new mutated forms of the H5N1 virus have emerged, principally in China, that have rapidly replaced earlier variants across SE Asia. Most recently a new “recombinant” virus has been detected in Cambodia and is associated with an unprecedented surge in human cases during 2013. Other new variants of the virus have proven to be no longer susceptible to existing poultry vaccines raising concerns that current H5N1 vaccines stockpiled for human use in the event the AI virus becomes an efficient human-to-human transmitter may be no longer efficacious. Mindful of the need for vigilance, USAID, under EPT-2, will continue its efforts to build on its successes while further consolidating our AI programs in the highest risk countries for maximum impact.

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In this context, “maintenance” refers to persistence of a virus within animals, people, or the environment.
2. Pandemic Preparedness In response to a growing concern about the possibility of an influenza pandemic and its potential to cause tens of millions of deaths, particularly in developing countries, USAID launched a series of efforts beginning with the *Humanitarian Pandemic Preparedness Initiative* (H2P) in 2007, a partnership with the U.S. Department of Defense’s Pacific and Africa Combatant Commands (PACOM and AFRICOM) in 2008, and in 2009 the *PREPARE* project to support national capacities (civilian and military) to prepare for and respond to the worst consequences of a pandemic. USAID focused its assistance to support national authorities to put in place pandemic preparedness plans that addressed five distinct areas:

- supportive care and treatment for those with influenza;
- limiting transmission from patients with influenza to others in their households and communities;
- provision of preventive and/or curative care for those ill with potentially fatal diseases other than influenza, e.g., malaria, diarrhea, bacterial pneumonia, other vaccine-preventable diseases, AIDS, tuberculosis;
- ensuring ready access to food; and
- rapid resumption of income-generating activities following a pandemic.

Underlying USAID’s approach to pandemic preparedness was the recognition that while all nations could be affected by an influenza pandemic, developing countries will likely have limited access to lifesaving vaccines and pharmaceuticals and as a result will be among the most vulnerable. Unlike the aftermath in more common large-scale disasters, access to aid (supplies and manpower) from traditional donor countries could be very limited or even non-existent while the ‘industrialised world’ struggled against the pandemic within its own borders. In countries where health systems are often not available in poor or remote areas, stockpiling supplies is either extremely complex or simply impossible for people at, or below, subsistence levels. When faced with more immediate threats to daily existence, inevitably, preparing for an influenza pandemic too often takes a low priority.

At the core of USAID’s pandemic preparedness agenda was ensuring that local populations can access and benefit from realistic and sustainable ‘off-the-shelf’ pandemic preparedness plans which district and community leaders have the capability to implement. To assure pandemic
preparedness plan sustainability, individual projects were designed to integrate into existing programmes – either health or disaster preparedness – at the community level in the target countries.

USAID’s pandemic preparedness work has been critical in enabling more than 25 countries (principally in Africa and Asia) that are at disproportionate risk of the consequences of a global influenza pandemic. USAID also strengthened the capacities of regional bodies such as ASEAN for the purpose of supporting the development of detailed “whole of society” national pandemic preparedness plans that emphasis the role of non-pharmaceutical strategies in protecting vulnerable populations. These plans, tested under simulation exercises highlighted the roles and responsibilities of key stakeholders from government (civilian and military), civil society and non-governmental organizations, and the private sector in responding to a pandemic. In 2009, in the face of the H1N1 pandemic virus, the national Pandemic Preparedness Plans proved extremely valuable in mobilizing an early and effective response to the anticipated threat of this novel virus in many of these countries. In 2011, the lessons learned from USAID’s pandemic preparedness work was captured at the Towards a Safer World Conference4 and set the stage for harmonizing this work with the UN’s International Strategy for Disaster Reduction and its Hyogo Framework for Action (2005-2015).

3. The Emerging Pandemic Threats Program  In 2009, recognizing the threat of new infectious diseases extended beyond the risks posed by avian influenza, USAID launched the Emerging Pandemic Threats (EPT-1) program. EPT-1 was designed to give earlier insight into the emergence of new public health threats (in addition to influenzas) and enhance country-level capacities to mitigate their potential impact. The EPT-1 portfolio initially drew heavily from the experiences and lessons acquired from efforts to address the threats posed by H5N1 – and as such reflects a strategic approach that (1) builds on the understanding that the future well-being of humans, animals and the environment are inextricably linked, (2) promotes a One Health approach that spans the animal health, public health, conservations communities and the environment, (3) targets promotion of those policies and the strengthening of those skills and capacities critical for both minimizing the risk of viral spillover, amplification, and spread and the ability to limit their social, economic and public health impact, (4) uses a “risk”-based approach to target investments where the likelihood of viral spillover, amplification, and spread is greatest.

EPT-1’s Strategic Approach provided a framework for USAID investments intended to reduce the risk of spillover, amplification, and spread of new viruses of animal origin and their potential economic and human toll. At the heart of EPT-1’s approach has been the recognition

4  http://towardsasaferworld.org/sites/default/files/tasw_conference_report.pdf
that to be effective USAID cannot be successful on its own and must partner with a range of other US government agencies, multi-lateral, bi-lateral, national, non-governmental, and private sector players. EPT-1’s strategic approach has been guided by the following assumptions:

- All populations are vulnerable to new viruses emerging in other countries; it is in our collective interest to strengthen the capacity of all high-risk countries to prevent the spillover, amplification, and spread of these new viral threats;
- Deadly zoonotic disease threats will increase steadily in the coming decades driven by population growth and expanded interactions between people, animals and the environment;
- Measures are currently available that if properly deployed could greatly reduce the risk of new virus spillover, amplification, and spread and their impact;
- It is possible, in the event of new virus spillover, amplification, and spread, to minimize its potential economic and public health impact through enhanced surveillance and early deployment of control measures; and
- Enhanced coordination across animal, human, and environmental sectors will contribute to reduced risk of new virus spillover, amplification, and spread and lead to early and effective control minimizing their impact should they emerge.

At the country level, the EPT-1 partners have been working with governments and other key in-country, regional and international partners to enhance the understanding of distribution of specific “high-consequence” viral families\(^5\) across “high risk” animal populations\(^6\) and key drivers of viral spillover, amplification, and spread—from deforestation and land use change to wildlife trade and livestock product demands. This information, along with other EPT-1 investments to strengthen country-level capacities for routine infectious disease detection and outbreak response, have been used to improve surveillance and response as well as risk-mitigation strategies\(^7\). Over its life, EPT-1 has significantly refined our understanding of the “drivers” that underlie viral spillover, amplification, and spread as well as established important new partnerships and platforms for even more timely and effective prevention, detection, and control of future threats.

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\(^5\) “High-consequence” viral families include those that have (1) at least one member known to infect animals and humans and (2) at least one member that can spread from person to person (with or without a vector) or have previously caused a pandemic.

\(^6\) “High-risk” animal populations include those with high contact rates with people and/or relatively high numbers of shared zoonotic viruses between the animals and people. Based on analyses by the PREDICT project under the EPT-1 program, “high-risk” animal populations include non-human primates, rodents, and bats.

The “Legacy” of EPT-1. EPT-1 is a suite of four capacity-building projects (PREDICT, PREVENT, RESPOND and IDENTIFY) that individually and collectively have made significant contributions to national, regional and global capacities to “detect, prevent and respond to” emergent threats. Below are the “End of Project” deliverables expected by the end of EPT-1 for each of the major lines of work supported:

- Viral Discovery
- Risk Characterization
- Risk Mitigation
- Early Detection
- One Health Capacities
- Outbreak Response

Viral Discovery: To address the need for early discovery of new, emergent disease threats the EPT-1 program, through its PREDICT component, has brought together a coalition of experts from wildlife ecology, genetics, virology, informatics and veterinary medicine focused on building a global early warning system for emerging diseases. Advances in genomics and informatics have allowed for investing in collecting genetic and epidemiologic data that tracks changes in select viruses for the purpose of developing a first generation “predictive model” for disease emergence. With its focus on detection and discovery of zoonotic diseases at the wildlife-human interface PREDICT has made significant contributions to: strengthening surveillance and laboratory capacities for monitoring wildlife and people in contact with wildlife for novel viral agents that may pose a significant public health threat; characterizing human and ecological drivers of disease spill-over from animals to people; and, strengthening and optimizing models for predicting disease emergence. By the end of EPT-1 the following deliverables will have been achieved:

- 100 percent of the target countries ⁸ will be capable of conducting appropriate animal sampling in key interfaces;
- 100 percent of target countries will have the capacity and/or access to diagnostics to test at least some of the 20 targeted high-consequence viral families;
- Surveillance data for all target countries will be incorporated into the global predictive model; and
- Initial characterization of viral and wildlife species diversity in target countries.

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⁸ EPT-1/PREDICT “target” countries: Africa – Cameroon, Democratic Republic of Congo (D.R. Congo), Republic of Congo, Gabon, Rwanda, Tanzania, Uganda; Asia – Bangladesh, Cambodia, China, Indonesia, Laos, Malaysia, Nepal, Thailand, Vietnam; Americas – Brazil, Bolivia, Peru.
Risk Characterization: A key part of USAID’s EPT-1 program has been the characterizing the biologic profile of specific high-consequence viral families circulating in animal populations as well as human behaviors and practices that are associated with their potential “spill-over, amplification and spread”. These investments have allowed for a better appreciation that the risk of viral spillover, amplification, and spread is ultimately determined by the interplay between the “biological risk” and the “behavioral risk”. As a consequence, a potentially deadly virus in an animal population that never interacts with human populations is ultimately little to no consequence to humans (at least while current conditions remain unchanged). It is in the understanding of “how, where and when” a potential viral threat circulating in animals will interact with human populations (or their domestic animals) that is key to determining what constitutes a genuine risk to public health. By the end of EPT-1 the following deliverables characterizing risk will have been achieved:

- A first iteration of a global model linking land use change, agricultural intensification, livestock production, extractive industries, and climate change to viral spillover, amplification, and spread in place;
- Initial characterization of risks associated with different animal-human interfaces completed, including transmission pathways associated with historical and current zoonotic outbreaks;
- A working model for monitoring “spill-over” of novel pathogens into humans in a limited number of sites;
- Longitudinal profiling of wildlife trade in a limited number of urban/peri-urban African markets;
- Initial monitoring of viruses on wildlife farms in at least one country; and
- A completed “Africa Livestock Futures” assessment focused on likely livestock production scenarios through 2030 and the potential for increases in zoonotic disease “spill-over, amplification and spread”, along with policy and regulatory options for risk mitigation.

Risk Mitigation: As the “risk mitigation” arm of EPT-1, PREVENT has focused on developing strategies for mitigating the risk of disease “spillover”. PREVENT has contributed to a significant increase in our understanding of options for mitigating the risk associated with those practices and behaviors (e.g. habitat change associated with “extractive industry”, bush meat hunting and butchering, raising wildlife for trade and consumption, and the marketing of animals) that expose people to zoonotic diseases. End-of-project deliverables include:
A “risk assessment/mitigation tool” for the Extractive Industry will have been tested in multiple mining sites;

Fora for routine policy-level dialogue with the extractive industry (mining and petroleum) will be established;

Policy framework for minimizing the risks associated with “wildlife farming” in SE Asia will be formulated in at least one Asian country; and

Through FAO, strategies and practices for mitigating the risk of viral spillover, amplification, and spread in poultry “value chains” in Asia will be validated.

Early Detection: As part of EPT-1’s overall strategy to be able to detect early new threats, IDENTIFY, a partnership between WHO, FAO and OIE, has focused on strengthening laboratory capacities to safely diagnose and report common animal and human pathogens. IDENTIFY has been instrumental in improving laboratory assessment tools that allow for better targeting of technical support and training; developing and rolling out training modules on diagnosing highly-infectious diseases; improving laboratory management practices related to biosafety and biosecurity; "twinning" labs with developed country labs; and expanding monitoring of antimicrobial resistance rates among priority pathogens. Additional support was provided to WHO’s Global Influenza Surveillance and Response System (GISRS), to expand its efforts to strengthen laboratory influenza diagnostic and reporting capacities in the Africa region. Through PREDICT significant effort was made to upgrade laboratory capacities in viral characterization. Among expected deliverables by the end of EPT-1 are:

• 31 human health labs and 39 animal health labs in 20 EPT-1-countries in Africa and Asia have enhanced capacities in safe handling, diagnosis and reporting of major endemic human and animal diseases;

• 25 laboratories in 20 EPT-1-focus countries have enhanced capacities in handling, detecting, and genetically characterizing known high-consequence and novel viruses in wildlife;

• Seven labs in the African region have enhanced capacities in influenza diagnosis and reporting as part of WHO/GISRS;

• National and local public health workers and laboratory staff trained in detecting, reporting, diagnosing and responding to disease threats of zoonotic origin (Uganda, DR Congo, and Indonesia); and

• Strengthened Viral Hemorrhagic Fever surveillance in Uganda.
**One Health Capacities:** Through a strategy that focuses on the central role of local Universities to train professional cadres of leaders responsible for supporting, promoting, and implementing the One Health approach, RESPOND has enabled the networking of 28 schools of public health, veterinary medicine, medicine and environment in both Africa (OHCEA Network\(^9\)) and Southeast Asia (SEOHUN\(^{10}\)). In addition, SEAOHUN partner countries have established national-level One Health networks involving an additional 45 schools. Working closely with their government counterparts, the university networks ensure not only that the skills they teach will meet the workforce needs of the nations’ ministries, but also that these skills are empowered in the workplace. Our One Health capacity-building strategies also included support for the public health and veterinary Field Epidemiological Training Programs of FAO, with particular focus on targeting animal health specialists. Expected deliverables by the end of EPT-1 include:

- OH University networks in Southeast Asia and Central/East Africa spanning 28 schools of public health, veterinary medicine, medicine and environment are in place;
- An additional 45 schools in Vietnam, Malaysia, Thailand and Indonesia are actively engaged in national-level One Health networks that draw from the lessons and materials of the regional network;
- Among the topics targeted are:
  - using an agreed-upon set of core professional competencies to develop course content and learning experiences to help students understand how animal-based diseases are evolving and spreading,
  - applied, field-based training programs, and
  - teaching and learning methodologies to improve collaboration across disciplines so that professionals are equipped with the skills needed to respond to outbreaks, and to build and manage cross-disciplinary teams.
- Functional Field Epidemiology Training Programs (FETPs) that strengthen in-service capacity for human and animal health and laboratory professionals in DRC, Uganda, Indonesia, Thailand, Cambodia, Laos and Vietnam.

**Outbreak Response:** One of the major lessons learned under EPT-1 is that timely and effective response “to events of public health significance” is frequently undermined by the absence of clear guidance on how to determine the underlying etiology of the event when it is unknown. While agent-specific guidelines are available for the response to public health events of known etiology, such as yellow fever and cholera, there has been a significant gap in written guidance for the early

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\(^9\) The One Health Central and East Africa (OHCEA) network includes universities from Uganda, Tanzania, Rwanda, Kenya, Ethiopia and D.R. Congo.

\(^{10}\) The Southeast Asia One Health University Network (SEOHUN) includes universities from Thailand, Vietnam, Malaysia, and Indonesia.
phases of recognition, reporting, investigation and response when the agent is initially unknown and the cause may be due to an infectious agent, environmental toxin or other factor. The absence of guidance has led to initial responses that are often chaotic and ineffective; it also means any “after-action” review is compromised by the absence of clear performance standards. To address this “gap” RESPOND supported an intensive process led by the WHO and included the participation of the Global Outbreak and Response Network (GOARN) network to develop and field validate a “tool” to be used by national authorities for identifying, investigating and responding to public health events of initially unknown etiology. More than a half dozen countries in Africa, by the end of EPT-1, will have been able to adapt this tool and develop National Outbreak Preparedness Plans – which describe the steps and the roles and responsibilities of national and international partners in responding to the initial signal of an event of public health significance. Importantly, this experience has laid the foundation for elevating outbreak preparedness planning as a major effort under EPT-2. Among the deliverables expected by the end of EPT-1 are:

- Comprehensive Public Health Event (PHE) Preparedness tool developed and field-validated with WHO and the GOARN network;
- The PHE Preparedness tool is incorporated as a core element of WHO outbreak preparedness strategy; and
- Up to seven countries in Africa have developed national preparedness plans using this tool.

**EPT-plus** The emergence in 2009 of the novel H1N1 pandemic virus in Mexico, after circulating and evolving undetected for over a decade in swine populations underscored a serious gap in global surveillance operations – the monitoring of swine livestock for future influenza threats. It is well established that swine can serve as “mixing vessels” for different influenza viruses from swine, poultry, migratory waterfowl, and people. Where animal production systems allow for the “free-flow” of influenza viruses between the different animal species, the recombination of influenza viruses in swine is thought to play a critical step in the evolution of new influenza viruses with human-to-human transmissibility. However, monitoring of influenza virus evolution in swine, particularly for variants which are asymptomatic or only cause mild symptoms in this host, has long been inhibited by fear of economic losses if new viruses are found and international regulations which only require notification of infections when there is evidence of severe illness or death among swine.

While not originally envisioned during the design of EPT-1, what became known as EPT-plus started in 2011 as a *proof-of-principle* to demonstrate that it is possible to routinely monitor swine and other livestock populations under production settings that have characteristically
diverse influenza profiles due to less-than-ideal application of biosecurity measures. Implemented by FAO with initial support from CDC, EPT-plus is actively working in China and Vietnam to: 1) conduct influenza surveillance in farmed animal systems where virus diversity is considered to be highest (e.g. swine, aquatic waterfowl, backyard poultry) and where biosecurity is imperfect; 2) implement surveys to assess biosecurity, animal movements, and epidemiological and animal production characteristics in the systems sampled; and 3) gather detailed information (e.g. sub-type and genetic sequence) for viruses present in these populations to better understand the dynamics of influenza virus evolution in swine and begin to identify “progenitor” influenza viruses that have not yet emerged as public health threats.

EPT-2: Building on AI and EPT-1’s Operational Platforms, Institutional Partnerships and Expanded Knowledge-Base

EPT-2, as with its predecessors AI and EPT-1, is focused on mitigating the impact of novel “high-consequence pathogens” arising from animals through a suite of One Health investments with the goal of enabling: early detection of new disease threats; effective control of new threats through enhanced “national-level” preparedness; and, a reduction in the risk of disease emergence by minimizing those practices and behaviors that trigger the “spillover, amplification, and spread” of new viruses. EPT-2 has the distinct advantage of being able to build on those “operational platforms” built or strengthened under Avian Influenza, Pandemic Preparedness, EPT-plus and EPT-1, as well as the technical partnerships and knowledge generated by these efforts to more effectively “prevent, detect and respond” to emerging disease threats.

EPT-2: Strategic Areas of Focus

Like its predecessors, EPT-2 has three overarching purposes: (1) prevention of the spillover, amplification, and spread of new zoonotic viruses; (2) early detection of new viruses when they do emerge; and (3) their timely and effective control. Under EPT-2 previous AI/EPT-1 work will be refined and/or expanded. EPT-2 will build on the lessons and knowledge from its predecessors and bring heightened focus to those places and practices that enable not just spillover of new viral threats, but potentiate their evolution, amplification and spread. At the

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11 “Operational platforms” are defined as public or private institutions or bodies in developing countries where the EPT-2 program will likely be active that may serve as implementers under the EPT-2 program. Examples of operational platforms are One Health coordinating committees, National Task Forces for infectious diseases, laboratories such as ICDDR,B (in Bangladesh), and networks of universities such as OHCEA or SEOHUN. To improve sustainability, EPT-2 will look to strengthen the capacity of operational platforms in targeted countries.

12 Technical partners include U.S.-based (e.g. DOD, USDA), international (FAO, OIE, WHO), and developing-country technical organizations.

13 “Evolution” is defined as the accumulation of genetic changes over time through random mutations and/or viral recombination.
same time, EPT-2 will invest in the One Health policies and capacities needed for prevention and control of viral evolution, spillover, amplification, and spread. At the core of EPT-2 are seven new areas of strategic focus:

1. **Developing longitudinal data sets for understanding the biological drivers of viral evolution, spillover, amplification, and spread**

   Under EPT-1 significant progress was made in identifying the primary wildlife reservoirs involved in “spill-over” of new viral agents and in the profiling of those viral families and some of their genetic variants most commonly circulating in these animal populations. Under EPT-*plus* important progress was made in describing how the interplay between genetics and ecosystems contributes to the evolution of new influenza variants. Under EPT-2 heightened focus will be brought to expanding these efforts by developing longitudinal datasets spanning select high-consequence viral families and their ecologies for the development of models describing the drivers and dynamics that underlie the evolution, spillover, amplification, and spread of new viral variants. Under EPT-2 EPT-*plus* will further refine its scope to address the evolution, spillover, amplification, and spread of new influenza variants. Collectively, this information will be critical to better forecast future threats and further target resources to where the risk is greatest.

2. **Understanding the human behaviors and practices that underlie the risk of “evolution, spillover, amplification and spread” of new viral threats**

   EPT-1 and AI were important windows for appreciating the central importance of “amplification” and “spread” for a new viral pathogen to pose a significant public health threat. When “spill-overs” involve human populations living in remote, poorly connected geographic areas the end result is frequently an “epidemiologic dead-end”. For a new viral agent to pose a significant public health risk the “spill-over” event must be closely linked to conditions which favor the further “amplification and spread” of the virus broadly among human populations. Under EPT-2 particular focus will be brought to identifying those geographic areas where the risks of “spill-over, amplification and spread” are greatest and characterizing those behaviors and practices that underlie viral evolution, spillover, amplification, and spread.

3. **Promoting policies and practices that reduce the risk of virus evolution, spillover, amplification, and spread**

   Under AI and EPT-1 it became increasingly clear that efforts to promote individual behaviors that were intended to lower infection to “rare” disease threats were highly ineffective. At the core of the dilemma was the common and accurate perception that the risks posed by
potentially new infectious diseases were very unlikely to affect any one individual. As such, there was little to no motivation for individuals to adopt new behaviors. On the other hand, it became increasingly clear that mitigating the risk posed by new infectious diseases could be more effectively addressed by focusing on policies and regulations that can affect the population-based behaviors and practices that contribute to “spill-over, amplification and spread”.

Under EPT-2 there will be particular focus on promoting policies and regulations that can impact on industrial and/or community scale practices that directly or indirectly contribute to “spill-over, amplification and spread” of new infectious diseases. EPT-2 will not focus on individual behavioral change and/or communications work. Under EPT-1 four areas were identified that can directly contribute to such risk, and these will be specifically targeted under EPT-2:

- **The Extractive Industry** (mining, petroleum, logging, and agri-business) is closely associated with dynamics and practices that contribute to habitat change, changes in population settlements, and increased population mobility – three factors critical to triggering the “spill-over” of a new infectious disease in remote “hot spot” areas and its “amplification and spread” into highly connected population settlements.

- **Urban/peri-urban markets** in Africa and Asia that actively market wildlife and wildlife products from remote “hot spot” areas to populations living in high density, globally connected locations.

- **Livestock “value chains” in Asia**: A major driver in the evolution, spillover, amplification, and spread of new viruses, particularly influenzas, in Asia over the past several decades has been the unabated co-circulation and mixing of novel viral strains among wildlife, poultry and swine, largely potentiated by livestock value chains.

- **Africa Livestock Futures**: In Africa, the absence of large scale animal production has limited the role of livestock value chains in potentiating viral intermingling of the kind documented in Asia. Dramatic changes in household wealth, exemplified by increasing GDP across Africa, are likely to lead to rapid increase in the demand for animal products and, as a result, increased livestock production. An unmanaged increase in production, as occurred in Asia in the 1960s -90s, could bring adverse consequences. The risk of disease-causing pathogens moving from wildlife into domestic animal populations is significant given the reservoirs of pathogens in African wildlife. This “risk”, however, is preventable if increases in livestock production incorporate well-established biosecurity measures. Under EPT-2 (Preparedness and Response) the promotion of policies and regulatory practices consistent with known animal husbandry “best practices” will be a major focus.
4. Supporting national One Health platforms

Under AI and EPT-1 it became clear that sustained and successful One Health practice requires that a broad range of government and non-government stakeholders come together and stay engaged in the collaboration as part of a normative practice, not just during the period when responding to an immediate infectious disease threat. By way of example, USAID has supported national governments in Africa to establish One Health plans or “road maps” to introduce and/or strengthen cross-sectoral collaboration. A number of countries had initiated cross-sectoral One Health collaboration when AI spread to the region. However, when it became apparent that the virus was not taking hold in the region the incentive for cross-sectoral collaboration faded. Under EPT-1 USAID expanded the scope of its support to address the broader threat posed by zoonotic diseases. This in turn has contributed to the ongoing One Health dialog among stakeholders in focus countries and has supported the university network to engage directly with government partners.

The experience from existing One Health Platforms is that they are most effective when they are country-owned and have been officially recognized or sanctioned by the national leadership (e.g. President, Prime Minister, or coordinating Ministry). The role of the One Health Platform is generally one of strategic planning, promoting a positive policy environment, information sharing, assessing national capacity for One Health engagement, and harmonizing systems. More specifically, the One Health Platforms serve as a focal point for assessing One Health capacities and a clearinghouse for new information, technologies, and opportunities. One Health Platforms are also well-placed to facilitate cross-sectoral dialogue related to One Health policies and or human resource issues; coordinate disease outbreak response; harmonize disease surveillance systems; share data on priority pathogens; identify and fill gaps in One Health workforce capacity; develop and implement a One Health strategy and/or zoonosis prevention and control plan; and plan or coordinate One Health-related research.

Under EPT-2 focused effort will be made to facilitate and support the formation and/or strengthening of One Health Platforms in the EPT-2 focus countries. Particular emphasis will be to support those efforts that play a catalytic role of advancing cross-sectoral

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14 National One Health platforms are formal groups of senior technical and administrative government representatives from a broad range of sectors who meet on a regular basis to coordinate and collaborate for improved health within each sector and for the prevention and control of zoonotic diseases. At a minimum, a national One Health platform will be composed of public health, animal health, and environment/wildlife ministry representatives. As appropriate and based on the country context, a platform should include additional ministries (e.g. trade, travel and tourism, economic, internal affairs, mining and natural resources, etc.), parastatal organizations (e.g. national laboratories, research institutes, etc.), universities, the private sector, and multilateral and bilateral stakeholders (e.g. WHO, FAO, USAID, CDC, World Bank, Red Cross, non-governmental organizations, etc.). In some countries the national One Health platform will have a policy making role or the platform will advocate for formation of supportive policies.
collaboration, promoting measures and/or practices that mitigate the risk of viral evolution, spillover, amplification, and spread, sharing of data and best practices, enhancing country preparedness for outbreaks of new or emerging infectious diseases and zoonoses, harmonizing cross-sectoral surveillance, honing cross-sectoral response skills, and/or leading to new opportunities to assess and strengthen related capacities.

5. **Investing in the One Health workforce**

Under EPT-1 our experiences with the “prevention, detection and response” of disease outbreaks reveal that the traditional skills, approaches, and relationships are inadequate to address the risks the world faces. Recognizing that most emerging diseases evolve through a complex interplay between animals, humans, and the environment, professional skill sets and practices must reflect that complexity, enabling collaboration across disciplines to stop diseases from becoming significant crises – an approach to disease prevention called “One Health”. However, since professionals are often educated and work in discipline “silos”, they are often less likely to engage one another in problem solving, even during disease outbreaks.

Under EPT-1 we have come to appreciate that universities play a critical role in creating long-term changes to workforce skills. As the primary educators of all health and science professionals, universities are a key catalyst in this transformation. They are working on the cutting edge of their fields, educating students who will comprise tomorrow’s workforce. Universities are also testing sites for education, where innovative and trans-disciplinary approaches to training professionals are constantly introduced and refined, including One Health approaches. By investing in universities in developing countries, we are creating a long-term capability for improved human resource capacity.

Under EPT-2 we will build on the One Health University Networks of Africa and Asia to target the long-term workforce needs for an effective implementation of One Health preventive, detection and response capacities. Under EPT-2 we will work closely with university partners and national governments to define national One Health workforce needs and strategies for their realization.

6. **Strengthening national preparedness to respond to events of public health significance**

Under the International Health Regulations all member states of the World Health Organization (WHO) are required to achieve core capacities for preventing, responding to, and reporting on Public Health Events of International Concern (PHEIC). A key activity under EPT-1 has been to support WHO, particularly its regional offices in Africa and in the Western Pacific, to develop and test the guidance document for preparing for and responding to
Public Health Events of Unknown Etiology. Under EPT-2 expanded support will be provided to assist EPT-2 target countries in the Africa and Asia regions to apply this guidance in the development and implementation of National Preparedness Plans for responding to PHEIC. This work will be done in concert with interagency efforts to develop national-level Emergency Operation Centers, including the Defense Threats Reduction Agency (DTRA).

7. **Strengthening global networks for real-time bio-surveillance**

Under EPT-1 and AI we invested in several distinct streams of laboratory strengthening. Through IDENTIFY we strengthened 31 human health labs and 39 animal health labs in 20 EPT-countries in Africa and Asia capacities in safe handling, diagnosis and reporting of major endemic human and animal diseases; through PREDICT we targeted 25 laboratories in 20 EPT-focus countries for enhanced capacities in handling, diagnosing and characterization of known high-consequence and novel viruses in wildlife; and, through WHO’s Global Influenza Surveillance and Response System (GISRS) we targeted seven labs in the Africa region for enhanced capacities in influenza diagnosis and reporting. Under EPT-2 we have the opportunity to expand the potential impact of these capacities by aligning our laboratory investments against the following strategic priorities:

(a) **A global database of respiratory pathogens:** Over the past half-decade WHO's GISRS has made significant gains in expanding the global reach of its influenza surveillance network, particularly in the Africa region. Further, by strengthening its linkages to clinic-based Influenza-Like Illnesses/Sever and Acute Respiratory Influenza (ILI/SARI) sites they have begun collecting important data sets that will enable better real-time monitoring of the evolution of influenza viruses. Importantly, influenza viruses are implicated in a minority of samples tested. In 2013 only 14% of all influenza-like samples tested by GISRS laboratory network in Africa were influenza positive. As such, the ILI/SARI samples provide an important window into understanding what "non-influenza agents" might be implicated in causing ILI/SARI. Under EPT-1 coronaviruses, which have been implicated in two respiratory-like illnesses, SARS and MERS, were shown to be much more virally diverse and geographically distributed than previously thought - the question remains as to whether they are playing a much larger role in routine respiratory illness. Under EPT-2 we will look to more strategically align our "viral discovery" and "influenza monitoring" activities to build a more longitudinal profiling of respiratory illness and underlying etiologies.

(b) **Enhanced biosafety and biosecurity:** An important objective of the laboratory work supported under EPT-1 has been in the promotion and adoption of practices and capacities that ensure the safe handling of dangerous pathogens. Under EPT-2 we will
build on this work and include the active promotion of multi-sectoral approaches for managing biological materials to support diagnostic, research and bio-surveillance activities. This effort will target the promotion of biosafety/biosecurity through our training and laboratory partnerships.

(c) Linking bio-surveillance data to response: The emergence of automated electronic information systems for monitoring, organizing, and visualizing reports of global disease outbreaks according to geography, time, and infectious disease agent has greatly enhanced the early identification of events of public health significance, even in areas relatively outside the reach of traditional global health efforts. With the rapid uptake of mobile information technologies, even in communities once considered beyond the reach of the modern information grid, these "IT portals" have the potential to play an increasingly important role in redefining the relationship between "providers and users of information" and in linking bio-surveillance data to response. Under EPT-2 we will explore options for how the One Health University networks, working in collaboration with the well-established WHO and CDC event-based surveillance systems, can better prepare their graduates to be active "providers and users" of these IT platforms, how our support for national "event preparedness planning" can incorporate these information nodes into their "early warning triggers", as well as explore how One Health policy reforms can better harmonize the flow of information from these portals with those of more traditional health surveillance systems.

**EPT-2 Geographic Focus**

Under EPT-1 the geographic focus was broadly around historical geographic “hot spots” where new microbes of animal origin had spilled over into human populations, specifically: the Americas; Central and East Africa; and South and Southeast Asia. EPT-2 will consolidate the GHSD portfolio around “hot spots” in Central and East Africa, and South and Southeast Asia, with heightened focus on the following EPT-2 priority countries (spanning AI and other emerging threats): Africa – Cameroon, D.R. Congo, Republic of Congo, Egypt, Ethiopia, Gabon, Kenya, Rwanda, Tanzania, Uganda; Asia -- Bangladesh, Cambodia, China, Indonesia, Laos, Malaysia, Myanmar, Nepal, Thailand and Vietnam. Much greater effort will be made to further
consolidate around those specific geographic areas within countries and “epidemiologic zones” where the risks of spill-over, amplification and spread are greatest.

EPT-2 Implementation Partners

As with EPT-1, EPT-2 will be composed of a suite of highly-integrated technical assistance projects and partners (see below) that draws from across the private sector, universities and non-governmental organizations. These projects and partners will share an overarching strategic vision and will collectively span the seven "Strategic Areas of Focus" (SAF) described above. Importantly, no one project or partner will be exclusively responsible for achieving any one of the SAFs. As was the case under EPT-1, the work of the projects and partners will be highly interconnected and interdependent. USAID will manage the relationships across EPT-2 to maximize the synergies and the shared effectiveness of the entire EPT program.

EPT-2 partnerships will include the following:

1. International and U.S. Government partners to include:
   
   • **WHO**: WHO will be active in four of the strategic areas of focus: strengthening real-time bio-surveillance (WHO/GISRS), particularly in supporting a global database of respiratory pathogens; strengthening the national preparedness to respond to events of public health significance (WHO/Africa Regional Office, WHO/Western Pacific Regional Office, WHO/GISRS); supporting One Health national platforms (WHO/Headquarters and regional offices); and, investing in One Health workforce (WHO/Headquarters and regional offices).
   
   • **FAO**: FAO will be actively involved in five of the strategic areas of focus: developing longitudinal datasets for understanding biological drivers of influenza virus evolution, spillover, amplification, and spread (FAO/EPTplus); promoting policies and practices that reduce the risk of influenza virus evolution, spillover, amplification, and spread (FAO/Headquarters and FAO/Regional Asia Program); supporting national One Health platforms (FAO/Headquarters and regional offices); strengthening national preparedness to respond to events of public health significance (FAO/Headquarters and regional offices); and strengthening global networks for real-time bio-surveillance (FAO/Headquarters and regional offices).

15 Defined as geographic areas within countries and/or across countries that are connected by movement of people, animals, or animal products and which have shared viruses (e.g. H5N1 Highly-Pathogenic Avian Influenza).
2. Technical assistance agreements\textsuperscript{16} that will be competitively awarded:

- **ONE HEALTH WORKFORCE (OHW):** This project will build on the partnerships forged through the One Health University Networks (i.e. OHCEA and SEOHUN) to address the workforce needs of national ministries and the private sector, as well as focus on strengthening the operational capacities of the university networks.

- **PREDICT-2:** This project will assist focus countries in identifying and monitoring "hot spots" for the evolution, spillover, amplification, and spread of animal viruses that are or may be pandemic threats. PREDICT-2 consolidates the research scopes of PREDICT-1 and PREVENT-1 from EPT-1 to more-precisely identify and characterize the zoonotic viruses in animals and people, as well as behaviors, practices, and conditions associated with viral evolution, spillover, amplification and spread.

- **PREPAREDNESS AND RESPONSE (P&R):** This project will assist focus countries to establish/strengthen One Health platforms through which they will develop and maintain highly functioning multi-sectoral collaboration. The Project will facilitate and support countries to develop and maintain exemplary cross-sectoral capacity and skills for responding to "public health events" at the regional, national, and subnational levels.

3. Local platforms and institutions in target countries that will be identified by USAID, the international partners, and the consortia that are awarded the OHW, PREDICT-2, and P&R projects.

**EPT-2 and the Global Health Security Agenda**

In early 2014, the United States joined in an international effort in the launch the Global Health Security (GHS) Agenda. At its core the GHS Agenda recognizes infectious diseases, whether naturally caused, intentionally produced, or accidentally released, are among the foremost dangers to human health and the global security. Limited capacity in many countries to prevent, detect, and rapidly respond to these threats, and the added danger of terrorists using biological material and expertise to achieve their own objectives, are among the key reasons for a concerted international effort at a senior leadership level to accelerate progress toward GHS. The GHS agenda elevates nine objectives\textsuperscript{17} that are aimed at preventing, detecting, and responding to biological threats; eight of these objectives are closely aligned with those of EPT-2.

\textsuperscript{16} The scopes, required skills, and expected results of these competitively-awarded projects are described in the three individual Requests For Applications.

\textsuperscript{17} \url{http://www.globalhealth.gov/global-health-topics/global-health-security/GHS%20Agenda.pdf}
At the core of both EPT-2 and the GHS Agenda is a strategic approach that fosters developing multi-sectoral collaboration with partners across public health/medicine, science, agriculture/veterinary, interior (security), border and trade, and defense agencies. As EPT-2 is implemented every effort will be made to ensure it is maximally coordinated with other US government agencies, national governments and international partners towards achieving the GHS Agenda objectives.