

# Terms of Reference for Request for Proposals

## First Fleming Fund Country Grant to Laos

### 1 Overview of this grant

This is a Request for Proposals (RFP) for the first Country Grant to address critical gaps in surveillance of antibiotic-resistant bacteria in Laos. It has been created in response to a Request for Support from the Government of Lao PDR. The grant will be funded by the UK Department of Health and Social Care, under its Fleming Fund Grants Programme, which is managed by Mott MacDonald, the Management Agent.

This first Fleming Fund Country Grant for Laos will focus on putting in place the foundations for antimicrobial resistance (AMR) and antimicrobial use (AMU) surveillance in the human and animal health sectors. It will facilitate a stronger One Health approach to surveillance bringing together multi-sectoral stakeholders to share surveillance data and gain a better understanding of AMR and AMU.

In the human health sector the grant will invest in the development and implementation of an AMR and AMU surveillance system, aligned with investments by the World Health Organization (WHO)/ Korea International Cooperation Agency (KOICA), Mérieux Foundation, and the UK's Wellcome Trust. In the animal health sector the grant will align with investments by FAO to support implementation of the new AMR and AMU surveillance plan for animals.

The Grantee will be responsible to Mott MacDonald for all aspects of the grant, including the management of any partners, their performance, technical delivery and financial accountability. The Grantee will be expected to sign the Grant Agreement and will be expected to enter into sub-granting arrangements with partners on the same back-to-back terms.

The Grantee will need to work in close coordination with the Antimicrobial Resistance Surveillance and Control Committee (ASCC), better known as the AMR Committee, as well as Mott MacDonald and other national stakeholders. The Grantee will also be required to harmonise efforts on this Country Grant with other types of grants under the Fleming Fund Grants Programme, namely Regional Grants and the Fleming Fellowship Scheme.

This grant is expected to last 18-24 months, and subsequent grants may be made available for later years. Support to Laos is expected to be for up to four years in total. Grant applications are expected to be in the region of £1-2 million, including all capital and recurrent costs, overheads and management costs.

## 2 Overview of the Fleming Fund

### 2.1 Introduction

The UK Government has established the Fleming Fund to respond to the global threat of drug-resistant infections, also known as antimicrobial resistance (AMR). The Fleming Fund will be a critical tool in achieving the resolution of the 68th World Health Assembly, 2015 (WHA A68/20), and in realising the ‘Political Declaration of the High-Level Meeting of the United Nations General Assembly (UNGA) on Antimicrobial Resistance, 2016’. These recognise that urgent cross sectoral rationalisation of antibiotic use and prevention and control of infections in humans, animals, food, agriculture, and aquaculture sectors are key to tackling AMR and calls for: innovative research and development; affordable and accessible antimicrobial medicines and vaccines; improved surveillance and monitoring; increased governance on antimicrobial use; and increased international cooperation to control and prevent AMR.

The Fleming Fund aims to address critical gaps in surveillance of antibiotic-resistant bacteria in low- and middle-income countries (LMICs) in Asia and Sub-Saharan Africa. Countries in these areas are set to bear the highest burden of antibiotic-resistant infections. A Global Action Plan on Antimicrobial Resistance (AMR) has been developed by the World Health Organization which acts as the blueprint for a multi-stakeholder global response to averting a global health crisis caused by AMR.<sup>1</sup>

The Fleming Fund comprises a number of workstreams. One workstream provides support to the Tripartite Alliance – the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (OIE) and the World Health Organization (WHO) – as part of the ‘One Health’ approach. Through funding to the Tripartite Alliance, the Fleming Fund has contributed to the development of National Action Plans in Sub-Saharan Africa, South and South-East Asia, and to the building of the evidence base and guidance for AMR surveillance. This work will be critical for the overall success of the Fleming Fund Grant Programme and underpins the delivery of the portfolio of Country and Regional Grants and Fleming Fellowship Scheme, as these will target capacity gaps identified in National Action Plans. The Fleming Fund also funds initiatives in academic institutions to develop guidance on the development of AMR surveillance systems.

The Fleming Fund Grants Programme is the largest stream of financial support available through the wider Fleming Fund. The UK Department of Health and Social Care has appointed Mott MacDonald as the Fleming Fund Management Agent for the Fleming Fund Grants Programme. Mott MacDonald is a global company with expertise in multi-sectoral international development and fund management. On behalf of the UK Government, Mott MacDonald is responsible for funding allocation and oversight of all investments made across the whole portfolio of grants in different activities in different countries.

The aim of the Fleming Fund Grants Programme is to improve the ability of recipient countries to diagnose drug-resistant infections, with an emphasis on antibiotics, and improve data and surveillance, to inform policy and practice at national and international levels. The overall goal is to avert the human and economic burden of AMR.

The geographic focus of the Fleming Fund Grants Programme is 20-24 LMICs from Sub-Saharan Africa, and South and South-East Asia. It will provide financial support over a five-year period from 2017 to 2021 to participating countries via three funding channels:

- Country Grants
- Fleming Fellowship Scheme Grants
- Regional Grants

Resources may also be available to conduct Operational Research on selected topics within these funding channels. These studies will provide an opportunity to better examine implementation ‘blockages’ or

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<sup>1</sup> <http://www.who.int/antimicrobial-resistance/global-action-plan/en/>

undertake more detailed case study analysis in themes of interest (e.g. value-for-money) for programme learning and adaptation purposes.

The Fleming Fund will be independently evaluated and Itad, a specialist evaluation firm, has been appointed by the UK Department of Health and Social Care for this purpose.

## 2.2 Problem statement to be addressed by the Fleming Fund

The main issues to be addressed by Fleming Fund Country Grants are outlined below:

- There are too few trained microbiologists to undertake the volume of testing required for representative surveillance on AMR.
- There are few health facilities that routinely undertake bacterial culture; still fewer facilities that meet the requirements for accreditation, or who do routine antimicrobial drug sensitivity tests.
- Routine AMR in healthcare delivery is not practice or there is no culture of surveillance for AMR in healthcare delivery and there are barriers to developing it.
- There is little perceived use of surveillance data on any level including low demand for the data from policy makers.
- There is a lack of knowledge on the use and consumption of antimicrobial agents across One Health sectors.
- There is a lack of antimicrobial stewardship.
- Logistical challenges are significant – transporting samples in a safe and secure manner under challenging transport conditions; ensuring a quality assured and sustained supply chain for reagents and consumables; and ensuring appropriate servicing of equipment are a few examples.
- Surveillance systems (national, regional and global) that do exist are often vertical in nature, are not linked, and are often unwilling to integrate.
- There are weak One Health structures and poor inter-sectoral collaboration.
- There is a heterogeneous picture across countries and regions in terms of starting points, political will, capability and donor interest and engagement.
- There are poorly defined and applied quality assurance standards in lab testing.
- There is lack of understanding from basic surveillance of pathogens on transmission patterns and drivers such as inappropriate use of antimicrobial drugs across all sectors.

## 2.3 Fleming Fund investment areas and outputs

To address the problems above, the Fleming Fund Grants Programme invests in:

- Laboratory infrastructure enhancement.
- Human resource strengthening and workforce reforms.
- Surveillance systems strengthening.
- Building foundations for AMR surveillance data use.
- Promoting rational use of antimicrobial medicines.

Investment in these areas is expected to achieve the following outputs:

- Improved laboratory skills and conditions for bacterial identification and Antimicrobial Susceptibility Testing; and therefore, improved data quality.
- Strengthened One Health workforce with a range of relevant skills for AMR surveillance.
- Stronger AMR surveillance systems and processes at country and regional levels.
- Stronger demand for AMR data at regional, country, subnational and facility levels.
- Better knowledge of country level patterns of practice and use of antimicrobials (particularly antibiotics) across sectors.

Fleming Fund outputs are expected to contribute to the following country outputs:

- Increase in quality and quantity of AMR data collected.

- AMR data shared in country to support evidence based policy and practice.
- AMR data shared internationally to improve and inform the global response.

The RFPs for Country Grants have been designed to ensure that investments and activities contribute directly to outputs. Grantees are expected to adhere to and demonstrate this alignment and contribution to outputs in their applications.

## 2.4 Core principles within the Fleming Fund Grants Programme

The Fleming Fund is built on four core principles. Grantees are expected to demonstrate how they will align with these principles while implementing the grant.

- 1) Country Ownership:** The Fleming Fund Grants Programme will work closely with national governments to ensure that country plans and aspirations, as laid out in their National Action Plans, are implemented; we will consult and work hand-in-hand with national governments to agree the approach and ensure sustainability. Grants and RFPs will conform to national priorities outlined in the National Action Plan and as articulated during Country Assessment visits. Unless there are good reasons to do so, Fleming Fund grants will chiefly invest in public sector laboratories and surveillance systems, thereby supporting national public health systems.
- 2) One Health:** The Fleming Fund recognises that the problem of AMR is a great danger to human health and cannot be controlled without a One Health approach. A specific set of One Health investment parameters has also been developed and is summarised below. This approach is aligned with key documents and guidelines from OIE<sup>2</sup> and FAO<sup>3</sup> as well as the Global Action Plan.
  - a. Collaborative multi-sectoral governance of AMR:** Leadership and resourcing of AMR surveillance and mitigation measures in all sectors that contribute to the emergence of AMR.
  - b. Integrated AMR and antimicrobial use and consumption surveillance in all sectors:** Surveillance in humans, livestock, aquaculture, crops, food and the environment to produce information that is interpreted by multi-sectoral teams to help understand factors associated with AMR emergence within and between sectors
  - c. AMR mitigation policies and programmes prioritised across multiple sectors:** Evidence-based policies and programmes for AMR mitigation measures that are prioritised across the relevant sectors, based on information generated through AMR and AMU/C surveillance in all sectors.
- 3) Alignment of Approach:** The Fleming Fund Grants Programme will seek to invest in areas which complement and build on work done to date, rather than create new systems. Grant applicants will need to demonstrate that they understand other actors' work in the field of improved laboratory capacity (both within and outside the sphere of AMR surveillance), improved disease surveillance, and the One Health approach. The Fleming Fund Grants Programme will assess grants for duplication of efforts and/or the development of parallel systems. To the extent possible, prospective Grantees will need to demonstrate how their proposals add value to existing and planned investments and systems.
- 4) Sustainability:** The Fleming Fund Grants Programme will focus assistance on national systems with a view to long-term sustainability. Investment size and scope should, as far as possible, be aligned with national government spending so that systems created with Fleming Fund grants are sustainable within the public health system. We also recognise that the public good of conducting AMR

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<sup>2</sup> OIE Standards, Guideline and Resolution on Antimicrobial resistance and the use of antimicrobial agents;

<sup>3</sup> The FAO Action Plan on Antimicrobial Resistance, 2016-2020.

surveillance means medium- to long-term support, and it is expected that countries that demonstrate good performance will have access to additional funds to provide ongoing support.

## 2.5 Fleming Fellowship Scheme

The Fleming Fellowship Scheme is part of the broader Fleming Fund Grants Programme, and is also managed by Mott MacDonald. Fellowships will provide grants to fund an 18-24 month programme of structured learning, mentoring and skills development for four to eight Fellows in each investment country. Rather than duplicate basic training, the Fellowships will focus on building advanced skills and leadership to promote the application of best practice in identified 'Beneficiary Institutions'. Beneficiary Institutions are organisations that add strategic value and complementarity to achieve the Fleming Fund's aims in the country and are likely to derive sustainable benefit from the Fellowship activities, such as AMR reference laboratories, national epidemiology units, hospitals and/or national drug administration agencies

The initial focus will be on strengthening quality of laboratory diagnostic data and the analysis and use of AMR and AMU surveillance data in Beneficiary Institutions. The scheme will support individuals and institutions to build the sustainability of programmes that seek to address AMR. The data they generate will be applied to deliver evidence-based approaches to tackling AMR, for example to improve antimicrobial stewardship.

Each country's national AMR committee, with Mott MacDonald, will determine the priority areas to be supported through Fellowships and the Beneficiary Institutions under the Fellowship Scheme. Each Fellowship will be matched with a 'Host Institution' from a preselected pool. When these have been decided, the Fellowship application process will open. Following selection, each Fellow together with their Beneficiary and Host Institutions will develop a budgeted work plan which will be agreed and funded by the Fleming Fund through the Host Institution.

Activities will include mentoring, secondments, participation in collaborative projects and specialised training that will support the Fellows within their workplace. These institutions will also support Fellows' workplaces to allow Fellows to implement what they have learned.

We expect this process to run in parallel with the selection of the Grantee for the Country Grant, which will enable the Grantee and the Host Institutions to align their work programmes.

## 2.6 Fleming Fund activities in Laos to date

This is the first RFP for a Fleming Fund Country Grant to be released in Laos. In preparation for this grant, Mott MacDonald carried out a Scoping Visit in January 2018 which was followed, in March 2018, by Positioning Activities (assessments) in a small number of public health laboratories and the National Animal Health Laboratory (NAHL).

Key stakeholders in the animal and human health sectors have been consulted throughout the process, including UN agencies and other development partners. This is to assist in alignment of Fleming Fund grant investments with other proposed activities. Scoping and Positioning identified major gaps and needs for strengthening AMR and AMU surveillance in humans and animals, identified other key stakeholders working in AMR and AMU surveillance, including WHO and FAO, and informed agreement with the Government of Lao PDR about grant objectives and outputs in line with Laos' National Action Plan for Antimicrobial Resistance.

## 3 The current AMR situation in Laos

### 3.1 National Action Plan for AMR

Laos has a draft 'National Action Plan (NAP) on Antimicrobial Resistance (2017 – 2020)' which is close to endorsement by the National Assembly. The 'National Emerging Infectious Diseases, Public Health Emergencies and Health Security Workplan (2016-2020)', developed with the support of WHO, also provides an important framework for antimicrobial resistance (AMR) activity and provides more detail of proposed activities; however, this is only partially funded.

The National Action Plan describes the AMR Surveillance and Control Committee (ASCC), better known as the AMR Committee, which predominantly represents the human health sector, with the Chairperson of the committee being the Director-General of the Department of Communicable Disease Control (DCDC) in the Ministry of Health (MoH). According to the Ministerial Agreement on the set-up of the AMR committee (No 3156/MoH, dated 30 November 2015), there is a subcommittees for overall matters, a subcommittee for technical matters, and a Secretariat.<sup>4</sup>

### 3.2 One Health

The approach to One Health in Laos, specifically cooperation between the MoH and the Ministry of Agriculture and Forestry (MAF) in response to zoonotic disease, has largely focused on emergency disease outbreaks. There is a Memorandum of Understanding (MoU) between the MoH and MAF which guides a coordination mechanism between the human and animal health sectors during these emergencies. There has also been cooperation between the human and animal health ministries in the early years of the highly pathogenic avian influenza pandemic; a zoonotic disease committee involving the DCDC and NAHL and Division of Veterinary Services (DVS); an annual One Health symposium; an annual joint celebration of World Rabies Day; twice-yearly laboratory coordination meetings; and joint simulation exercises.

The challenge for the Government of Lao PDR now is to take a wider view of One Health as it relates to the slower burning problem of AMR and to institutionalise integrated One Health AMR surveillance. A One Health approach is stated in the "National emerging infectious diseases, public health emergencies and health security workplan (2016 – 2020)". This serves as a common framework to coordinate health security activities in line with International Health Regulations (IHR) and as such it captures planned activities in the animal and human health sectors. Funding to support these activities is very limited. The Government of Lao PDR has stated its intention to develop links and an approach for collaboration across sectors, and the Fleming Fund Grantee will be expected to support these initial steps (see Objective 1).

### 3.3 AMR Surveillance – human health

Laos is in the early stages of defining its approach to AMR surveillance. The WHO Country Office has received a four-year (2017 – 21) US\$1.8 million grant from KOICA (via WHO headquarters in Geneva) to develop and implement AMR surveillance in Laos and has done some initial work with government staff to map out the approach.

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<sup>4</sup> Subcommittee responsible for overall matters: 12-members. Provides overall guidance and support in terms of technical and financial resources needed to implement activities for the surveillance and control of AMR; consolidates data and information; conducts meetings for sharing lessons learned.

Subcommittee responsible for technical matters: 10-members. Consolidates data and information from implementation; researches findings; performs surveillance and control of AMR; provides technical support; collaborates with stakeholders; organize and participates in training; conducts meetings; attends quarterly meetings; reports on implementation of AMR activities to the secretariats for consolidating and further reporting.

Secretariat: - 5 members from MoH. Consolidates data and information submitted by the technical subcommittee; facilitates AMR coordination; organises training and meeting; conducts quarterly meetings; monitors and manages budget and materials for the implementation of AMR activities; consolidates findings and reports to the subcommittee responsible for overall matters and MoH.

(ref: Ministerial Agreement on the set-up of the AMR committee (No 3156/MoH, dated 30 November 2015)

Proposed outcomes to achieve improved laboratory and epidemiology capacity include: a defined national AMR surveillance system, established coordination of the national AMR surveillance system, a strengthened national reference laboratory in the National Center for Laboratory and Epidemiology (NCLE), established surveillance sites, and AMR data representative of the country produced and shared at national level and with GLASS; monitoring and evaluation of the system will also be set up.

Landmarks on the proposed timeline to achieve these outcomes include identifying AMR surveillance needs, assessing gaps in AMR surveillance core components and defining surveillance linkages (February 2018), establishing and defining the National Coordination Centre (March 2018), capacity building of national focal points, defining structures to coordinate the national surveillance system and developing TORs for surveillance sites (April 2018), developing a national surveillance protocol (July 2018) selecting surveillance sites (September 2018) and establishing/adapting systems, tools, infrastructure and processes in place at surveillance sites from November 2018. There is then the intention, in 2018, to develop a sampling strategy, expand surveillance sites, and develop and implement an M&E plan.

Activities planned for 2018 include: identifying focal points, mapping existing structures, resources and activities in identifying gaps, preparing for data collection, translating and adopting WHO protocols on AMC monitoring, interpreting and disseminating findings, setting up a sustainable AMC monitoring system, translating and adopting WHO protocols on AMU in hospitals and training on national AMC monitoring.

In 2019, data on AMC from importers and local manufacturers will be collected, training on the analysis and presentation of AMC data will be conducted, and AMC data and results will be reported to the national level and into GLASS. In 2020 – 21 there is a broad plan to select sites for AMU surveys among AMR surveillance sites, analyse and report results from the AMU surveys and evaluate IT platforms and host AMU data (e.g. DHIS 2) and continue monitoring AMC at the national level.

The WHO KOICA grant will fund three WHO posts in Laos to support implementation: an AMR Coordinator (international appointment, six months initially, posted in April 2018) who will coordinate and provide technical support in developing and implementing national AMR surveillance and a national antimicrobial stewardship programme; a microbiologist (international post, six months initially, expected to be in post in 2018) who will be based at NCLE to provide technical assistance; and a post which will provide technical support on laboratory testing (national post, one year, posted in May 2018).

WHO also has funding to support activities and procurement to improve capacity of NCLE and estimates that it can also support three surveillance sites. Mott MacDonald will work with WHO and the Government of Lao PDR to further specify support from the respective organisations during forthcoming missions, prior to the commencement of the grant, and currently planned for July 2018. The appointed Grantee will continue this close coordination to ensure ongoing alignment and coordinated planning.

### 3.4 AMR Surveillance – animal health

As of the beginning of 2018, the National Animal Health Laboratory (NAHL) had conducted antibiotic susceptibility testing (AST) on only a very few samples from diseased poultry and pigs (including carcasses). The AMR data from these tests has not been collated and analysed and the sampling frame is unclear, making interpretation difficult.

The Lao PDR AMR Surveillance Plan in the Animal Sector (2018 – 2020), (LASP-AH), was prepared in early 2018 with the assistance of FAO. Surveillance will initially focus on testing for resistance in select zoonotic and commensal bacteria carried by healthy food-producing animals. The Department of Livestock and Fisheries (DLF) identified swine and layer poultry as the most important livestock sectors for AMR surveillance in Laos, taking into consideration the production systems and the nature of antimicrobial usage. Surveillance will initially focus on swine with expansion to poultry in the future. District/provincial livestock officers will collect caecal samples from pigs at slaughterhouses in up to 8 provinces. Samples will be initially collected at provincial laboratories and transported to NAHL, which will process, isolate and test for resistance to a range of antibiotics in *Escherichia coli* and *Salmonella spp.* FAO has conducted training of NAHL and provincial staff in sample collection and bacterial isolation, with the expectation that sample collection and isolation will begin

about mid-2018. FAO will support this surveillance until the end of March 2019 with Fleming Funds received directly from the UK Department of Health and Social Care.

### 3.5 Laboratory capacity – human health

The NCLE in Vientiane is the designated national reference centre for AMR. The role of the laboratory is to provide diagnostic and confirmation facilities, to provide oversight and training to low-level facilities, and perform research. NCLE takes part in several international EQA programmes including the UK NEQAS Vaccine Preventable Diseases and the New Zealand based Pacific Paramedic Training Centre's Microbiology EQA. However, NCLE requires improved capacity to fulfil its role. It conducts AST on samples collected during investigation of reportable disease outbreaks, but reports on its ongoing, sustained role in quality assurance of subordinate laboratories are mixed. AMR data has not yet been analysed and NCLE requires assistance to improve its capacity to undertake analysis.

The 18 provinces in Laos each have a provincial hospital with a laboratory. AMR sentinel sites are envisaged to be at the central and provincial level initially, with a view to expand the network to all levels. Fourteen provincial hospitals currently have the capability to perform culture and simple identification of bacteria.

Lack of trained staff is a major constraint in all the laboratories. There are no clinical microbiologists in Laos outside of the Lao-Oxford-Mahosot Hospital Wellcome Trust Research Unit (LOMWRU), and there is a general shortage of trained laboratory technologists.

Availability and cost of reagents and consumables is a problem which was mentioned at all the hospitals visited by the Fleming Fund team. There are few providers of specialist laboratory reagents in country. In a recent change in policy, hospitals must now find the cost of these reagents from general funds and pass on these costs to patients making bacteriology tests expensive. Expiry of specialist reagent stock is also a problem. The time taken to order and receive consumables is reported to be between 6 weeks and 1 year; 3-6 months is reported to be typical if specialist reagents are ordered. The lag-time in the supply-chain encourages over-ordering which can lead to wastage of reagents with short expiry dates.

Lack of budget for maintenance and a shortage of biomedical engineers makes equipment certification, upkeep and maintenance a particular problem in Laos. There is little or no capability to service equipment so engineers have to be brought in from Thailand or further afield and is expensive and unsustainable. Given that much of the equipment is donated, there is little standardisation and donations seldom come with long-term plans for funding maintenance.

Maintenance of biosafety cabinets is of particular concern. NCLE is tasked with arranging this for all provincial labs but attempts to secure funding have not yet been successful. The last servicing was done in 2016, presenting a significant biosafety risk to laboratory staff and the environment. It is understood that WHO and DTRA will support the servicing of 20 cabinets for Biological Safety Cabinet (BSC) certification in 2018.

A particular biosafety problem in Laos is *Burkholderia pseudomallei*, the causative agent of melioidosis, which is frequently isolated from blood, urine and pus cultures. *B. pseudomallei* is a containment level 3 organism. Clinical diagnosis of melioidosis is difficult: it has been nicknamed "The Great Imitator" as it can have a wide variety of clinical presentations and can lie dormant for months or years. Untreated, fatality rates can exceed 80% in patients with septicemic infection and multiple foci.

### 3.6 Laboratory capacity – animal health

In 2012 the National Animal Health Center of the DLF was split into NAHL (diagnostic services) and the Division of Veterinary Services (DVS) which is responsible for disease control and surveillance and has an Epidemiology Unit. This has had an influence on the collaboration between the laboratory and the services under DVS.

The NAHL has been identified as the reference laboratory for the animal health sector. The NAHL is a well-equipped lab in a relatively new (2013) purpose-built four-storey building in Vientiane. The lab has been well supported to strengthen virology capability following the emergence of highly pathogenic avian influenza in Asia in the late 1990s. No support has been provided for bacteriology. The bacteriology laboratory tests approximately 3–7 samples per month, predominantly Rose Bengal test for brucellosis, with very few samples

cultured and even fewer samples tested for antibiotic sensitivity. A new campus is being built for the DLF outside of Vientiane, including a new, larger laboratory. Completion is proposed for 2020 at which stage the equipment from the current lab will be moved to the new lab. Setting up the new lab is expected to take about three months when there will be considerable disruption to diagnostic services.

The animal health laboratory network includes the NAHL in Vientiane and seven provincial laboratories located in: Phongsaly, Luang Namtha, Oudomxay, Luang Prabang, Vientiane Capital, Savannakhet, Champasak. The provincial laboratories conduct very minimal diagnostic testing and have no capability for culturing bacteria. They require support to become adequately equipped and trained in bacteriology.

The DLF has a plan to assess provincial animal health laboratories and develop a strategy during 2018 to strengthen one laboratory in the north, central and southern provinces to contribute to AMR surveillance.

As the laboratory techniques are broadly the same in both human and animal sectors, many of the laboratory issues mentioned above also apply to the animal health labs, e.g. lack of trained staff, reagents supply and equipment maintenance. The similarity of many aspects of surveillance means that joint solutions may be appropriate, for example training on laboratory techniques and quality systems, on data entry and analysis and sharing technicians for equipment maintenance.

A pilot mission using the FAO Assessment Tool for Laboratory and AMR Surveillance System (ATLASS) was conducted in May 2017 in Laos. A comprehensive report which outlines the critical gaps in the laboratory and overarching AMR surveillance programme has been transmitted to the DLF and can be considered a useful resource.

### 3.7 Rational use of drugs

There are multiple channels for accessing antibiotics for human use including widespread over-the-counter purchasing which means that there is no overview of the availability, source and quality of antibiotics. There is sporadic circulation of poor quality, counterfeit pharmaceuticals either produced in-country or imported.

The National Action Plan on Antimicrobial Resistance summarises research illustrating inappropriate antibiotic use with patients self-treating before seeking medical advice. There is no national guidance on antimicrobial drug use in Lao language, and there is a general proclivity towards antibiotic use among the general population, with limited law enforcement capacity for scrutinising imports and the private sale of drugs. There is a general expectation among both the public and prescribers that a fever requires the prescription of an antimicrobial medicine. The scale of the problem is magnified by user fees and the health system's dependence on revolving drug funds to support service delivery. Policy makers would benefit from a better understanding of antimicrobial consumption (AMC) and antimicrobial use (AMU) at the national, hospital and community levels.

Farmers have access to all classes of antibiotics, including the most recent and crucial ones for human treatments (ATLASS report, FAO 2017). DLF staff reported to the positioning activity team that there is currently no system for registering veterinary drugs imported into Laos and no legislation to restrict the use of antibiotics in animal feed. However, DLF has drafted Prime Ministerial decrees to address each of these issues. The decrees have been drafted in the Lao language and DLF hopes these will be passed about the middle of 2018.

## 4 Scope of this Country Grant

### 4.1 Grant Objectives and Outputs

Objectives and outputs for this Country Grant are summarised as follows. Section 7 provides more detail. It is expected that applicants will respond to this RFP by developing and proposing activities that are costed and by proposing appropriate indicators (see Section 9). All inputs must be permitted under the list of Eligible Funding Items, as outlined in Annex 1.

Objective/Output	Inception	Implementation
<b>Objective 1: Strengthened One Health approaches to information sharing</b>		
Output 1.1: Two national symposia on AMR and AMU delivered.	x	x
Output 1.2: Support the multi-sectoral sharing and comparison of AMR and AMU surveillance information within the technical subcommittee of the ASCC, and sharing of the key findings from AMR and AMU surveillance with the subcommittee responsible for overall matters in the ASCC.	x	x
<b>Objective 2: Strengthened AMR and AMU surveillance system in the human health sector</b>		
Output 2.1: National AMR and AMU Surveillance System Strategy developed.	x	x
Output 2.2: NCLE has increased capacity to act as the national AMR reference laboratory.		x
Output 2.3: Improved biosafety and biosecurity in NCLE and surveillance sites.		x
Output 2.4: Clinicians at surveillance sites (as identified in the surveillance strategy) demonstrate better understanding of AMR surveillance protocols, antimicrobial stewardship, and antimicrobial sensitivity data.		x
<b>Objective 3: Strengthened AMR and AMU surveillance system in the animal health sector</b>		
Output 3.1: Assessment of NAHL capacity needs and gaps complete.	x	
Output 3.2: NAHL produces reliable quality bacterial culture, identification and antibiotic sensitivity results for <i>Salmonella spp</i> and <i>Escherichia coli</i> .		x
Output 3.3: Biosafety and biosecurity in NAHL improvements made.		x
Output 3.4: Good quality samples from the agreed livestock species are regularly sent to NAHL from selected provinces for culture and AST.		x
Output 3.5: NAHL maintains an up-to-date and accurate database of the demographic details and matched culture and AST results for each sample collected in the AMR surveillance, using WHONET or similar appropriate software.		x
Output 3.6: NAHL maintains a secure and accurately inventoried national biorepository of all the isolates generated through AMR surveillance.		x
Output 3.7: DVS conducts epidemiological analysis of the AMR data, reports on quarterly and annual AMR trends in animals, and shares with DLF and the technical and general subcommittees of the ASCC.		x

Output 3.8: Strategy developed for strengthening three provincial animal health labs for AMR surveillance

x

## 4.2 Duration and phasing of the grant

The grant is expected to be implemented for 18-24 months.

The grant will be divided into two phases, an inception phase expected to last up to six months, and an implementation phase which will cover the remainder of the grant. The table above illustrates which outputs are expected to be delivered in which phase.

During the inception phase, the Grantee will:

- Complete or begin work on the Outputs, as outlined above.
- Collaborate with the Fleming Fellows and their Host Institutions to understand the Fellowship workplans.
- Develop a detailed budget and workplan for the implementation phase that is aligned with the Fellowship workplans.
- Agree an MOU with the Government of Lao PDR.

The remainder of the Outputs should be completed during the implementation phase, as outlined above.

Proposals for the grant will require a detailed budget and workplan for the inception phase; these activities need to be in line with government restrictions on what can take place while the project MOU is not yet finalised.

On the same budget and workplan template, proposals for the grant should also include an indicative budget and workplan for the implementation phase which should be detailed to the extent possible. At the end of the inception phase, the Grantee will be expected to revise and update their workplan and budget (including procurement) for the implementation phase, and will propose which standard indicators will be used to measure success (see Section 9). These will be subject to review by the Mott MacDonald's Core Technical Team and sign-off by Mott MacDonald.

The Grant Agreement will be signed on award of the grant, but the Grantee will need to agree an MOU with the Government of Lao PDR in order to carry out implementation activities. Mott MacDonald will assist with and provide support in developing and gaining approval for the MOU, but in the event that that the MoU is not granted, the Grant Agreement will be reviewed accordingly.

A second, subsequent Country Grant may be available to Laos, dependent upon successful implementation of the first Country Grant. This could be subject to another competitive tendering exercise and further assessments later in the grant funding period.

## 4.3 Funding envelope

Grant applications are expected to be in the region of £1-2 million, including all capital and recurrent costs, overheads and management costs.

The Fleming Fund wishes to see value for money in the form of maximum outputs for the grant money invested. The Guidance Notes for the Grant Application Form provides different dimensions that should be considered as part of a VfM approach – economy, efficiency and effectiveness – and an indication of how we may assess VfM.

## 4.4 Procurement

A procurement plan and budget should be developed by the end of the inception phase. Pending approval from Mott MacDonald, the Grantee would be expected to facilitate the procurement process. Their choice of procurement route may be subject to assessment by the International Procurement Agency (IPA), a partner of Mott MacDonald in the Fleming Fund Grants Programme providing advisory services.

## 4.5 The Fleming Fellowship Scheme in Laos

According to current plans, seven Fleming Fellowships, from both the human health and animal health sectors, will be issued in Laos. Successful applicants will receive specialised training in AMR and AMU data management and analysis, laboratory quality management, and advanced laboratory technical skills. Fellows are expected to become technical leaders in AMR and AMU surveillance in Laos, and it is hoped that they will play a role as mentors and active trainers in capacity building activities that will be implemented through this Country Grant. Therefore, once established, the Grantee is expected to work in collaboration with Fleming Fellows and potentially their Host Institutions (who provide remote support to the Fleming Fellows).

Summary terms of reference for all the Fellowships, currently under discussion with the Government of Lao PDR, are attached at Annex 2. It is our expectation that, by the time the Grantee can begin implementing the Country Grant, the Fellowships will be established.

It is important to note that training of other laboratory staff as specified below, should be designed and funded by the Grantee within this Country Grant application. The Fellowship Scheme is not designed to support training, but is a longer-term scheme to develop expertise and practice amongst individual fellows.

## 5 Key partnerships, alignment and coordination

The Country Grant must be delivered in a way which supports the national effort and which takes account of current capacity levels, absorptive capacity, alignment with others, and the particular challenges – cultural, political and linguistic – of working in Laos. The Grantee must also ensure that all inputs complement and build on work done to date and avoid duplication and development of parallel systems.

DCDC has expressed its desire for donor efforts to be coordinated and the Grantee is expected to be an active and supportive member of this arrangement, facilitating national leadership and ownership of the programme. The mechanism for coordinating the multiple donor inputs is not yet established, and therefore the Grantee must be prepared to work in a dynamic and evolving environment and be mindful of the need to coordinate with all parties at every opportunity.

In the human health sector the delivery approach and inputs must be closely aligned with national priorities, as stated in the NAP and the 'National Emerging Infectious Diseases, Public Health Emergencies and Health Security Workplan'. There must also be close alignment with inputs being provided by WHO and, where relevant, other development partners. This means that the Grantee, in addition to working closely with national stakeholders, must work closely with the WHO Country Office and WHO staff posted to NCLE during both the inception and implementation phases. Allocation of grant resources should support the national effort in a transparent way by specifying resource allocation in a workplan and budget that has been jointly developed by government officials, WHO, and the Grantee, where possible.

In the animal health sector the delivery approach and inputs must be aligned with the NAP, the 'National Emerging Infectious Diseases, Public Health Emergencies and Health Security Workplan', and the LASP-AH. Approach and inputs should also build on the components of this surveillance plan that are implemented with the support of FAO during 2018 until March 2019. The Grantee must work closely with both the DLF and the FAO National Consultant for AMR (on secondment from the NAHL) to agree on the target populations

(including livestock species and geographic areas) for AMR surveillance and confirm the focal bacteria for which antibiotic sensitivity is conducted.

Much of the success of this grant, in particular Objective 1, depends upon the ability of the Grantee to bring stakeholders from multiple sectors together and facilitate joint working. Close collaboration with a wide range of stakeholders at different levels in the Government of Lao PDR is central to the success of this grant. The Grantee will also need to build and leverage partnerships with several AMR stakeholders beyond those in government and the UN, to include academic, training and research institutions, the private sector, and other development partner-supported programmes.

The Grantee must particularly bear in mind the need to enable sustainability of AMR surveillance beyond the life of the grant. Prospective grantees will be expected to describe concrete strategies to promote sustainability of outputs in their proposals.

## 6 Complementing other grants from the Fleming Fund Grants Programme

The first Country Grant is expected to work effectively and synergistically with other grants under the Fleming Fund Grants Programme at the regional level. This relates to both the Fleming Fellowship Scheme (see Sections 2.5 and 4.5) and Regional Grants. The Regional Grants will focus on strengthening networking and data sharing on AMR at the regional level. The Grantee is expected to liaise, through Mott MacDonald, with such grants for maximising the sharing of AMR data and learning at the regional and global levels.

## 7 Detailed Objectives and Outputs

### 7.1 Objective 1: Strengthened One Health approaches to information sharing

#### **Output 1.1: Two national symposia on AMR and AMU delivered.**

Formal cross-sectoral working in Laos to achieve a One Health approach is challenging, and requires support to improve it. Therefore, the entry point for the Fleming Fund will be a focus on creating a neutral environment, such as a national symposium, that brings stakeholders from the multiple sectors and programmes together and promotes sharing of information generated through their programmes, with the aim of achieving a better understanding of AMR and AMU in Laos. Output 1.1 proposes two national One Health symposia on AMR and AMU, with the first symposium to be held within the first six months of the grant, to bring together the different groups (government and non-governmental) who are working on AMR and AMU in the human, animal and/or environment and agriculture sectors.

It will be an opportunity for participants to present on the AMR and AMU work they are doing and discuss their results to date with stakeholders from multiple sectors. It will help identify the different groups working on AMR and AMU, what they are doing and their approaches, which will help to align the activities of different groups and to share information. Ultimately it should lead to a better understanding of AMR in Laos. The intention is that this should be a high-profile event with a keynote speaker who is an internationally recognised expert in AMR plus invited local and international speakers and presentations that are submitted for oral and poster presentations.

The Grantee will be expected to work with the technical subcommittee and the Secretariat of the ASCC to organise the symposia under the overall leadership of the AMR committee. It will also be important from a One Health perspective that the Grantee facilitates coordinated leadership and oversight of the symposia by the line ministries concerned, MoH and MAF.

The second symposium should be held towards the end of the grant period, providing a focus for Fleming-funded participants and others to bring together the information generated through the programme, assess its

contribution to understanding AMR in Laos, present on lessons learned and recommend priorities for future work, which may be supported through a second Country Grant.

The Grantee's proposal should clearly specify which activities will take place during the inception phase, bearing in mind the restrictions of operating without an MOU.

By the end of the grant we expect that the following will have been achieved:

- Two symposia successfully delivered.
- Active participation in both symposia by the human and animal health sectors and wider AMR stakeholders.
- Improved cross-sectoral understanding of AMR and AMU in Laos.
- Findings provided to the ASCC.

**Output 1.2: Support the multi-sectoral sharing and comparison of AMR and AMU surveillance information within the technical subcommittee of the ASCC, and sharing of the key findings from AMR and AMU surveillance with the subcommittee responsible for overall matters in the ASCC.**

In Laos there is an acknowledged need to improve the quality, representativeness and comparability of surveillance data between the sectors to develop hypotheses regarding drivers of AMR. These hypotheses should then inform surveillance priorities which in turn should ultimately lead to the development of evidence-based policies to reduce the incidence of AMR. Once policies are in place surveillance systems need to collect data that monitors the effectiveness of the policies.

The entry point for the Fleming Fund will be to support the sharing and comparison of AMR and AMU surveillance information between sectors within the technical subcommittee of the ASCC.

The role of the grantee would also include, but not be limited to:

- Facilitating the ASCC to organise regular meetings of the technical subcommittee of the ASCC, and develop a ToR for members so they are clear about their responsibilities and the role of the subcommittee.
- Building capacity of members of the subcommittees to understand and interpret the results of AMR and AMU surveillance.
- Building capacity of members of the subcommittee to present evidence-based recommendations to the ASCC regarding policies and actions to facilitate responsible antibiotic use and reduction in AMR.
- Ensuring that the AMR and AMU surveillance information discussed during the meetings and the outcomes of the meetings are deposited with and securely stored by the ASCC.

The Fleming Fellowship Scheme proposes to support 3 of 7 Fellowships in the epidemiology units of the Department of Communicable Disease Control, the NCLE and the Division of Veterinary Services (see Annex 2). The Fellows will be expected to become technical leaders and contribute to sustained cross-sectoral sharing of results, and so the Grantee should facilitate their involvement in, or engagement with, the technical subcommittee.

The Grantee's proposal should clearly specify which activities will take place during inception, bearing in mind the restrictions of operating without an MOU.

By the end of the grant we expect that the following will have been achieved:

- The technical subcommittee of the ASCC is operating effectively and sustainably, with TORs outlining clear roles agreed for individuals and the group as a whole.
- Active participation by both the human and animal health sectors.
- Greater capacity within the technical subcommittee to understand and interpret AMR and AMU data.

- Sharing of surveillance results with the subcommittee of the ASCC that is responsible for overall matters, together with recommendations for future research priorities, programming and policies.

## 7.2 Objective 2: Strengthened AMR and AMU surveillance system in the human health sector

### Output 2.1: National AMR and AMU Surveillance System Strategy developed.

The role of the Grantee is to contribute to the development of the national surveillance strategy, primarily through the provision of technical assistance. As outlined above (see Section 3.3) and, as proposed in the NAP, the Government of Lao PDR is currently in the early planning stages of setting up a surveillance system for AMR, AMU and AMC. This is being supported by WHO. The Grantee is expected to contribute to this process, during inception and implementation, particularly focusing on AMR and AMU, by providing technical assistance, training and other support as appropriate, aligned with the needs of government and the contributions of WHO. Although it is noted that an assessment of NCLE is due to be completed by July 2018, the Grantee may also need to carry out detailed lab assessments in NCLE and potential surveillance sites to identify needs and gaps.

The Fleming Fund wishes to support international sharing of data. To this end it is encouraging countries to sign up to and provide data to WHO's GLASS database. Planning for surveillance should consider the 'priority pathogen' sample types, bacteria and antibiotics that the GLASS database is accepting. In addition, the inputs from the Grantee should be guided by the roadmap produced by the Fleming Fund: "AMR Surveillance in low- and middle-income settings - a roadmap for participation in the global antimicrobial surveillance system (GLASS)".<sup>5</sup> This can be used to complement other sources of guidance produced by WHO.<sup>6</sup>

By the end of the inception period, under the leadership of DCDC, the Grantee should have identified and agreed with Government and WHO, how the Grantee will contribute to the further development of the national surveillance strategy. These inputs will align with those from Government and WHO, ensure development of an agreed, sustainable surveillance system, and take account of absorptive capacity.

By the end of the grant we expect that the following will have been achieved:

- The National AMR Surveillance System Strategy drafted and costed. This will include clearly outlined clinical case definitions and laboratory methods.
- A costed operational plan agreed.
- A plan for AMC and AMU surveillance is developed.
- A monitoring and evaluation plan developed.
- The roles and responsibilities of all organisations contributing to the surveillance system clearly outlined.

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<sup>5</sup> AMR Surveillance in low- and middle-income settings - a roadmap for participation in the global antimicrobial surveillance system (GLASS). <http://amr.lshtm.ac.uk/wp-content/uploads/sites/12/2016/11/AMR-Surveillance-Protocol.pdf>

<sup>6</sup> GLASS – Manual for Early Implementation: <http://www.who.int/antimicrobial-resistance/publications/surveillance-system-manual/en/>

National antimicrobial resistance surveillance systems and participation in the GLASS – A guide to planning, implementation, and monitoring and evaluation: <http://www.who.int/glass/resources/publications/national-surveillance-guide/en/>

Diagnostic stewardship: a guide to implementation in antimicrobial resistance surveillance sites: <http://www.who.int/glass/resources/publications/diagnostic-stewardship-guide/en/>

Once the surveillance strategy has been developed and agreed the Fleming Fund may be open to further discussion about how the current, or a possible future, grant could support implementation, subject to an approved budget and workplan.

**Output 2.2: NCLE has increased capacity to act as the national AMR reference laboratory.**

NCLE has been identified as the national reference laboratory. A summary of its current capacity is outlined above. The Grantee is expected to support NCLE to take up its role with minimal delay. Inputs provided by the Grantee during the implementation phase must align with those which will be provided by WHO and those which can be covered by the Government. Prospective grantees, in their proposals, must identify strategies to ensure sustainability of NCLE's greater role beyond the life of the grant. Possible areas for support by the Fleming Fund could include:

- **Services.** Although the NCLE laboratory has a backup generator and a generally reliable power supply, it is still subject to power fluctuations. Much of the electrical equipment is not properly protected. The microbiology laboratory cannot currently make its own distilled water for media preparation and buys this in. It can be expected that surveillance will result in an increase in the amount of media being prepared, making a local distilled water source more important and cost-effective.
- **Bio repository.** A secure repository of isolates is an important asset to allow further investigations of the pathogens isolated. Purchase of ultra-low temperature (-80°C) freezers is needed. Before installation, power supply both on mains and back up sources should be considered. The repository needs to be inventoried and isolates need to have epidemiological data associated with them; NCLE has experience with the PACS software for this purpose (compared to NAHL) but this is not currently operational. Finally, there need to be clear policies for its use, for example which isolates get selected for banking, for how long they are retained, and how access is granted for their use.
- **Accreditation.** NCLE aspires to ISO 15189 accreditation. Accreditation is an important indicator of the quality of the laboratory. The Grantee should support this effort as it applies to the bacteriology section, but keep in mind realistic incremental steps towards accreditation.
- **Supervision.** NCLE needs to expand its supervisory role as a reference laboratory. This will include assisting NCLE in provision of SOPs and bench aids suitable for subordinate labs to use and supporting NCLE's provision of bacteriology EQA to its subordinate sites.
- **Training.** NCLE staff need to receive training in techniques that allow more detailed characterisation of pathogens and resistance mechanisms than the simple disc diffusion testing that they are currently conducting. This could include both phenotypic and genotypic methods. Wherever possible this should be practical rather than theoretical, based on samples in their collection. Given the limited human resource available at NCLE the scope of this work should be delivered at NCLE and at an agreed activity level.
- **Epidemiology.** The epidemiology unit at NCLE is strong but has no experience with handling AMR/AMU data. For the surveillance system to provide useful results the epidemiology staff will need training on AMR and AMU data analysis. Software (e.g. WHONET) that allows data entry and analysis will need to be installed and configured. IT systems that allow back up of data and input of data from subordinate labs should be considered.
- **Maintenance.** Maintenance of laboratory equipment is a problem in Laos. Most technical support for maintenance of most specialist laboratory equipment has to be sought from outside the country which increases the cost and leads to delays in repair. Of particular concern are the biosafety cabinets. Those in NCLE and the hospital labs were last serviced in 2016. This servicing is supposed to be arranged by NCLE centrally for all the provincial labs. NCLE is currently attempting to arrange funding to service all the biosafety cabinets at provincial hospitals alongside its own.
- **Supply of Reagents and Consumables.** It is important that the surveillance system has a reliable supply of consumables, which at the same time avoids oversupply and expiries. A mechanism to

ensure this should be explored. These may include stock control systems at the labs. It may also include working with key suppliers, preferably within the country, to ensure availability of stock.

- **Strategy for dealing with biosafety level 3 pathogens.** Given that *B. pseudomallei*, a biosafety group 3 pathogen, is regularly isolated from cultures in Laos, all laboratories should be properly equipped, staff should be trained, and procedures put in place for biosafety and biosecurity. (See also Output 2.3)

By the end of the grant we expect that the following will have been achieved:

- A secure, inventoried, biorepository system in place together with policies for its operation (e.g.: selection of isolates for saving, arrangement for accessing isolates, etc.)
- NCLE bacteriology section and biorepository has a reliable power and distilled water supply.
- Progress made towards ISO 15189 accreditation for the bacteriology lab.
- Training in advanced techniques for pathogen identification and antibiotic resistance mechanisms characterisation delivered.
- NCLE delivers quality support services in bacteriology to its subordinate labs including documentation, EQA, and confirmation of results.
- NCLE has decided on software for surveillance data and analysis, it has been installed and training delivered.
- All specialist laboratory equipment at the NCLE bacteriology lab has a maintenance plan in place and implemented.
- A plan for sustainable supply of bacteriology reagents and consumables developed.
- Agreed plans for handling dangerous pathogens in place and implemented.

### **Output 2.3: Improved biosafety and biosecurity in NCLE and surveillance sites.**

Following the planning and assessments carried out during inception, if necessary further training and other inputs should be provided by the Grantee to ensure long-term improvements in biosafety and biosecurity.

By the end of the grant we expect that the following will have been achieved:

- The lab is equipped with appropriate safety equipment and staff are wearing personal protective equipment while conducting testing.
- All biosafety cabinets are regularly maintained and calibrated. Staff have been trained on their use.
- All waste is disposed of in a safe manner.
- All staff are trained and supervised to the appropriate level for their job descriptions / roles
- Appropriate ongoing supervision of Biosafety and Biosecurity is undertaken by training and appointment of a Biosafety Officer.

### **Output 2.4: Clinicians at surveillance sites (as identified in the surveillance strategy) demonstrate better understanding of AMR surveillance protocols, antimicrobial stewardship, and antimicrobial sensitivity data.**

In the public hospital system in Laos there is limited use of the bacteriology laboratories to inform diagnosis and prescribing. This arises out of a lack of good-quality, timely microbiology services, limited knowledge of the value of the data among clinicians, the existence of revolving drug funds to support service delivery which incentivises over prescription, the cost of laboratory tests which is handed on to patients and reduces demand, limited infection prevention and control activities in hospitals, and widespread practice of self-treating which can reduce the ability of the laboratory to isolate the pathogen.

One way to mitigate some of these problems is to improve understanding among clinicians of the relevance of AMR to their work, the importance of antimicrobial stewardship and how to use antimicrobial sensitivity data. A successful surveillance programme in a hospital environment requires the clinicians to correctly identify patients fitting the surveillance criteria throughout the hospital. This is best achieved if clinicians are

thoroughly aware of the importance of surveillance to their patients, the hospital and the country generally. It is important that clinical staff understand the processes in the laboratory and some training on this should be included. Clinical and laboratory staff should be encouraged to interact so that they understand the pressures and limitations within which they operate. The Grantee will be expected to deliver capacity building and training for clinicians at the AMR the surveillance sites. This should be aligned with the national infection prevention and control programme as appropriate. The Fleming Fund has developed a roadmap for surveillance in low- and middle-income settings which is aligned with GLASS,<sup>7</sup> and which should be used as a guide to inform clinical surveillance. It is not expected that all functions would be developed during the life of this grant, but it is expected that significant steps would be taken towards standardised protocols used to guide selection of patients, laboratory tests undertaken, and use of the data in clinical practice.

In addition, where possible, the Grantee should ensure as much as possible that financial barriers to testing are mitigated. The Country Grant should be able to cover all costs related to necessary equipment, reagents, and consumables and there should be no costs to the patients for accessing the test required under the surveillance protocol.

By the end of the grant we expect that the following will have been achieved:

- Training provided on AMR surveillance protocols, antimicrobial stewardship, and antimicrobial sensitivity data to clinical staff at proposed surveillance sites delivered.
- Trained staff are able to correctly identify patients fitting the surveillance criteria and demonstrate an understanding of how to incorporate bacteriology results into their clinical practice.
- There is an increase in the number of samples collected and sent to the laboratory for microbiological analysis which is free at the point of use to patients.

### 7.3 Objective 3: Strengthened AMR and AMU surveillance system in the animal health sector

#### Output 3.1: Assessment of NAHL capacity needs and gaps complete.

It is hoped that by late 2018 the bacteriology lab at NAHL should be collecting isolates and ideally testing for AST for *E. coli* and *Salmonella spp.* for approximately 10 months, under the AMR surveillance programme supported by FAO (with financial support from the Fleming Fund). Concurrently, the Fleming Fellowship Scheme will support a Laboratory Fellow in NAHL to focus on strengthening laboratory quality systems (see Annex 2). The Fellow will be matched with a Host Institution which will provide a mentor with expertise in microbiology quality management systems. The Fellowship would cover training and mentoring for the Fellow in laboratory quality management. Note however that training of laboratory staff should be designed and financially covered by the Grantee within this Country Grant application.

By the beginning of the Country Grant, it is anticipated that Mott MacDonald will have worked with DLF and FAO to identify the priority livestock species and geographic areas for the AMR surveillance programme to be supported through the grant, and the type of data management and database for storing AMR surveillance data. The Grantee will need to ascertain if there are any issues with the quality of samples that have been sent from the field, in discussion with microbiology staff. Where issues are identified and where new areas are included in the programme, field staff will need to be trained in sample collection and transport methods. The Grantee will also need to conduct an assessment of data management and database requirements for storing AMR surveillance data, as well as the freezers and biorepository options at NAHL.

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<sup>7</sup> AMR Surveillance in low- and middle-income settings - a roadmap for participation in the global antimicrobial surveillance system (GLASS)

<http://amr.lshtm.ac.uk/wp-content/uploads/sites/12/2016/11/AMR-Surveillance-Protocol.pdf>

As outlined in Section 5, existing tools and plans should be considered, with a view to reducing duplication of planning and assessments.

By the end of the inception phase, the Grantee, aligned with FAO and in collaboration with the Fellow's Host Institution if appropriate and feasible, should complete the assessment of the following:

- the capability and quality of NAHL's diagnostic testing to support AMR surveillance and determine what additional training and guidance in diagnosis and quality systems is required.
- the capacity of NAHL to extend diagnostic testing to include new organisms beyond *Salmonella* and *E. coli* should also be assessed, with consideration given to whether culture and AST for the commensal organism *Enterococcus faecium* can be included in the panel of tests conducted under the AMR surveillance programme.
- if any laboratory equipment needs to be serviced and calibrated.
- biosafety and biosecurity capacity and needs.
- the quality of the samples sent in from the provinces for culture and AST.
- the data management and database requirements.
- the biorepository options at NAHL.

By the end of the inception period the Grantee should have identified and agreed with Government and also FAO, on the basis of these assessments, clear areas for support by the Grantee to deliver Outputs 3.2 - 3.8. Inputs must be aligned with those of Government and FAO and must take into account absorptive capacity and must promote long-term sustainability. These inputs will form the basis of the implementation workplan, budget and procurement plan to be agreed with Mott MacDonald(see Section 4.2).

**Output 3.2: NAHL produces reliable quality bacterial culture, identification and antibiotic sensitivity results for *Salmonella spp.* and *Escherichia coli*.**

Following the assessment during inception (Output 3.1), it is anticipated that during implementation the Grantee should then work with the laboratory to improve diagnostic and quality management capacity, as identified. Note that this training is separate to the Laboratory Fellowship training and is aimed at strengthening a broader group of laboratory technicians. It is likely that up to four staff will need further capacity building to improve their diagnostic techniques.

In order to produce reliable results, the Grantee will procure quality reagents and consumables, including media and antibiotic discs. This should include sufficient consumables and reagents to support testing of an agreed number of samples for *E. coli* and *Salmonella* plus an additional species of bacteria if it is to be included in surveillance during the lifespan of the Country Grant.

The Grantee will also procure and install the equipment that is required by the lab for quality microbiology testing. The Grantee will need to organise servicing of equipment, including the laboratory's generator and water pump, and will need to provide fuel for running the generator and the laboratory's incinerator.

Advice will be given to encourage the use of best laboratory standards for identification and antibiotic sensitivity testing including use of SOPs, monitoring of equipment and internal quality control checks on assays. The laboratory also needs to be supported to participate in a relevant and regular external quality assessment programme.

By the end of the grant we expect that the following will have been achieved:

- NAHL has an operational water pump, generator and incinerator.
- NAHL has the necessary equipment to safely conduct reliable culture, identification and AST, and the equipment has been serviced and calibrated to produce reliable diagnostic results.

- Microbiology laboratory staff produce reliable culture, identification and AST results for the agreed bacteria as assessed by a relevant external quality assessment exercise and by records of appropriate internal quality control.
- All samples from the surveillance programme have been processed as per protocols.

**Output 3.3: Biosafety and biosecurity in NAHL improvements made.**

Following the assessment during inception (Output 3.1), if necessary, further training and other inputs should be provided by the Grantee during the implementation phase to sustainably improve biosafety and biosecurity.

By the end of the grant we expect that the following will have been achieved:

- The lab is equipped with appropriate safety equipment and staff are wearing personal protective equipment while conducting testing.
- The biosafety cabinet is operational and being used by staff appropriately.
- All waste is disposed of in a safe manner.
- All staff are trained and supervised to the appropriate level for their job descriptions / roles
- Appropriate ongoing supervision of Biosafety and Biosecurity is undertaken by training and appointment of a Biosafety Officer.

**Output 3.4: Good quality samples from the agreed livestock species are regularly sent to NAHL from selected provinces for culture and AST.**

Following the assessment during inception (Output 3.1), the Grantee may be required to train field staff in eight provinces in epidemiologically robust specimen collection (including data collection) and transport methods. Training should be practical, involving hands-on experience collecting samples from a local slaughter plant, farm, food production facility(ies) or other appropriate locations. Similar training may already have taken place in March 2018 and this should be clarified during inception.

The Grantee will need to procure sufficient consumables and transport media for samples. The Grantee will also need to identify and implement the optimal process for the safe transportation of samples from the provinces to the NAHL.

By the end of the grant we expect that the following will have been achieved:

- District staff collect appropriate samples for AMR testing that are labelled appropriately, transported in a safe manner, arrive at NAHL in good condition for diagnostic testing, and are accompanied by appropriate epidemiological and demographic information that is labelled to match the samples.
- District staff have sent the required number of samples to NAHL for diagnostic testing.

**Output 3.5: NAHL maintains an up-to-date and accurate database of the demographic details matched to culture and AST results for each sample collected in the AMR surveillance, using WHONET or similar appropriate software.**

Following the assessment during inception (Output 3.1), appropriate software, such as WHONET, may need to be installed if no such software is in place, and staff may need to be trained in entering data into the system and sharing with the Epidemiology Unit of the Division of Veterinary Services (DVS) for epidemiological analysis.

NAHL does not have sufficient human resources to enter data generated through any of its programmes, including the AMR surveillance program. The Grantee will need to ensure that AMR data is entered and maintained in a secure database and plans need to be included to ensure the sustainability of laboratory reporting after the grant is finished.

By the end of the grant we expect that the following will have been achieved:

- Results for all samples tested under the surveillance programme are entered into WHONET or similar software, with laboratory results accurately matched to demographic details for each sample.
- Data is regularly backed up.

**Output 3.6: NAHL maintains a secure and accurately inventoried national biorepository of all the isolates generated through AMR surveillance.**

There are currently four -80°C freezers in NAHL. However, these have little spare capacity. Following the assessment (Output 3.1), the Grantee will need to support NAHL in maintaining a biorepository.

There are two possible options for generating freezer space:

1. Rationalise what is currently stored in the four -80°C freezers and see if any room can be created for the new bacterial isolates.
2. Purchase a new -80°C freezer for the bacterial isolates. Before purchasing, an assessment needs to be made to ensure sufficient power resources are available to support a further freezer alongside other essential equipment.

These options should be considered during the inception phase, as circumstances may have changed.

PACS is an inventory system that is currently in use in NAHL. This system could be used to maintain an inventory of the isolates in the freezer.

Laboratory staff would need to be trained in appropriate sample storage methods, labelling, and maintaining an inventory in PACS. This is likely to be covered under the Fellowship (with the Host Institution training the Fellow), but this will not be confirmed until the Fellow's workplan is agreed.

The Grantee will procure consumables and reagents necessary for storage of isolates.

By the end of the grant we expect that the following will have been achieved:

- All the isolates generated through the AMR surveillance programme are stored in a -80°C freezer using an appropriate storage method.
- All stored isolates are inventoried in PACS and can be readily located for further testing.

**Output 3.7: DVS conducts epidemiological analysis of the AMR data, reports on quarterly and annual AMR trends in animals, and shares with DLF and the technical and general subcommittees of the ASCC.**

It will be important to apply an epidemiological approach to analysing and reporting the results of AMR surveillance, particularly as the AMR surveillance in animals will be based on targeted surveillance of resistance in enteric bacteria carried by healthy animals, and hence will require a population-based approach to analysis. The relevant epidemiology unit is housed within the DVS, which is now a separate group to NAHL. Involving the DVS would help to build an AMR working group in the DLF, involving the NAHL, DVS and Veterinary Products focal point in the Vaccine Laboratory.

Analysis and interpretation of the AMR surveillance data will be supported by a Fleming Fellowship. It would be useful for the Grantee to support quarterly meetings with all contributors to AMR/AMU surveillance in DLF to share and discuss results and discuss issues re data supply, quality, etc.

By the end of the grant we expect that the following will have been achieved:

- DVS is producing results from analyses of the AMR surveillance data and sharing with NAHL, DLF and the technical subcommittee of the ASCC.

### Output 3.8: Strategy developed for strengthening three provincial animal health labs for AMR surveillance.

The DLF has a plan to assess provincial animal health laboratories and develop a strategy to strengthen one laboratory in the north, central and southern provinces to contribute to AMR surveillance.

The Grantee can support the assessment of these provincial labs and develop a strategy for the improvement of three of these labs. Implementation of this strategy could then be supported in the second Fleming Fund Country Grant.

By the end of the grant we expect that the following will have been achieved:

- Assessment of infrastructure, equipment needs and human resource capacity of the seven provincial animal health laboratories for bacterial culture, identification and AMR complete.
- Three provincial labs to contribute to the AMR surveillance network – north, central, south – identified
- Budgeted plan to strengthen the three laboratories so that they can perform culture, identification and AST for *E. coli* and *Salmonella* developed.

## 8 Lead Grantee Roles and Responsibilities

The main role of the Lead Grantee will be to plan and execute the 15 outputs and deliver the three objectives listed above. The Lead Grantee is responsible for providing, either through in-house resources alone, or through a partnership or consortium, the expert technical assistance and high-quality support needed to achieve agreed results.

The Lead Grantee is responsible for financial management and controls for the grant as a whole (including the contributions of sub-grantees if applicable) and for reporting to Mott MacDonald. Reporting of financial expenditure against budgeted activities is a requirement of the grant and grantee(s) will need to show evidence of sufficient capabilities to undertake these responsibilities.

The Lead Grantee is also responsible for monitoring and reporting on all activities under the grant as a whole (including the contributions of sub-grantees if applicable).

## 9 Measuring success

Country Grants are ultimately expected to generate results that can be tracked using a standard set of indicators that will monitor progress and achievements within and across Country Grants. A copy of the full list of indicators will be shared in the Application Pack.

However, Mott MacDonald recognises that, for much of this first grant, given the early stage of organised AMR surveillance in Laos, these indicators may not yet be applicable. Therefore, applicants are expected to select from the standard indicator set only where appropriate. Where it is too early to select and use indicators because results attainment is at the 'process' (and not 'output') level of results delivery, completion of activities (i.e. mapped by objectives) against agreed targets and time will be monitored.

In summary, while the completion and level of attainment for all activities requires monitoring, the type/level of activity will determine the monitoring method. When developing the application, applicants should:

- Select from the proposed indicators for activities, where appropriate. *Or,*
- Identify targets and timeframe completion for 'process' type activities (i.e. where indicators provided are not applicable /too advanced);

A mix of these options is also appropriate depending on application content. In the revised and updated workplan to be submitted to Mott MacDonald at the end of the inception phase, prior to implementation, the Grantee will be expected to revisit/confirm the monitoring plan which will then be agreed with Mott MacDonald.

In addition to measuring grant performance against the objectives and outputs stated above, the grant will also be monitored on the implementation of, and adherence to, the Fleming Fund core principles described in Section 2.4, and practical implications for this will be discussed with the successful applicant. No further action is required at this stage.

## 10 Application requirements

### 10.1 Grant Eligibility Criteria

Potential grant applicants must satisfy the following eligibility criteria before applications will be assessed in detail. Applicants:

- Must demonstrate that they are competent organisations responding to this call for proposals;
- Must have an appropriate track-record in supporting lab capacity development, surveillance, capacity building, and One Health.
- Must have experience of programme implementation in Laos.
- Must demonstrate that they are registered to work within the country, including the provision of essential documents such as articles of incorporation.
- Must demonstrate an understanding of the MoU process with the Government of Lao PDR.
- Must be prepared to accept the Grant Agreement terms.
- Must be able to provide the same information and assurances for all sub-grantees, where the application is from a consortia.
- Should be able to provide all information required for due diligence checks, including clear evidence of financial standing and systems of financial management and control.
- Should be able to provide evidence of suitability in the form of references from clients and donors for previous work undertaken within the last three years.
- Can be a single organisation or consortia, though the latter must clearly identify a Lead Grantee with the appropriate governance and coordination mechanisms to manage sub-grantees.
- Can be:
  - National institutes – such as a university or research institutes;
  - Non-governmental organisations (NGOs);
  - UN Agencies;
  - Private companies;
  - Government-owned enterprises or institutions, provided they can establish that they are (i) legally and financially autonomous, (ii) operate under commercial law, and (iii) are not dependent agencies of national governments

### 10.2 How to apply

The Applicant Information Session (AIS) will be organised in Vientiane for **11 June 2018**. The details of the venue will be shared with applicants who have registered their interest. Interest to attend the AIS must be registered by emailing [flemingfundSEA@mottmac.com](mailto:flemingfundSEA@mottmac.com) **by 4 June 2018**

Prospective grantees must register interest to receive the Application Pack by emailing [flemingfundSEA@mottmac.com](mailto:flemingfundSEA@mottmac.com) **by 12 June 2018**. Please include the organisations name, the name, phone number and email address of the main focal point.

Ahead of the event, an advance Application Pack will be shared and will include an application form, budget and monitoring template, and Guidance Notes. Following the Applicant Information Session, the **official Application Pack** will be sent out on 13 June 2018 to prospective grantees who have registered interest by the 12 June, as per the details above

To apply, please complete the application form and budget and monitoring template that will be provided, in line with the Guidance Notes.

Note the key requirements set out at the beginning of the Country Grant application form:

- Your submission should be returned by the deadline indicated in the RFP.
- When submitting the application document, press “Reply All” from the Application Pack automated email that you received on 13 June with the application documents attached. Do not send it to us from a new email, and do not modify the Subject-line. Only “Reply All” emails will register the documents in our system.
- Keep file sizes as low as possible - there is a 9MB size limit to each individual email that can be received by the grant submission software. You can submit documents by sending multiple emails attaching submission documents to each one. Please follow the instruction (above) using “Reply All” to the original email.
- Applicants should observe the word limit indicated for each question. Additional words outside the limit will be disregarded.
- All documents included as part of the proposal must be submitted in Word, Excel, and PDF format (body font: Calibri 11pt). Do not send through as zipped files.
- You should include a covering letter, signed by the person authorised to represent your organisation for the submission of this proposal.

Proposals that do not satisfy these criteria may not be accepted and may be returned.

### 10.3 Evaluation criteria

The Application Pack will include the application form, indicating the scoring and weighting for each section of the application. The Application Pack will also contain Guidance Notes explaining what we are looking for in terms of a good quality response for each question, including approach to Value for Money (VfM).

In particular we are looking for a Grantee / Grantees who can demonstrate its:

- technical capacity to address the different aspects of AMR covered by this Country Grant.
- ability and preparedness to bring stakeholders together in an effective and productive working arrangement, promoting a One Health approach.
- ability to operate effectively in Laos.

### 10.4 Restrictions/limitations

Any conflict of interest, or potential conflict of interest, should be declared to Mott MacDonald when applicants are registering their interest to apply for the grant. If a conflict of interest, or potential conflict of interest, arises after that point the prospective grantee must clearly declare this in their proposal.

### 10.5 Key dates

- Publication of RFP: 22 May 2018
- Registration to apply for the grant is open **between 22 May and 12 June 2018**.
- Deadline for registering interest to attend the Applicant Information Session: 4 June 2018 17.00 ICT (GMT+7).
- Applicant Information Session: 11 June 2018 – time TBC, Vientiane
- Deadline for registering interest to receive the official Application Pack: 12 June 2018 17.00 ICT (GMT+7).
- Application submission deadline: 20 July 2018 17.00 ICT (GMT+7).
- Anticipated start date of grant: 1 October 2018.

## 10.6 Contact details and support information

Any questions on the Request for Proposals should be sent to [flemingfundSEA@mottmac.com](mailto:flemingfundSEA@mottmac.com). Mott MacDonald will endeavour to respond to queries within three working days.

## Annex 1: Eligible funding items

### Laboratory Infrastructure Enhancement

- Infrastructure: renovation, redecoration, electricity and water supply, environmental controls, waste and waste disposal.
- Equipment: appropriate equipment for the level of capability; biosafety and biosecurity equipment; automated culture and identification platforms; IT equipment.
- Reagents, durables & consumables: appropriate media, reagents, culture plates, etc; glassware; sample collection consumables.
- Transport and logistics: vehicles or contracted services for transport of goods, and people; safe and secure transport of specimens and samples; logistical support for surveys.

### Human Resource Strengthening and Workforce Reforms

- Training: clinical, veterinary, agricultural and One Health surveillance protocols; biosafety and biosecurity; microbiology, laboratory science and laboratory management; epidemiology and surveillance; genomics; IT training.
- Long-term support: ongoing and refresher training according to the competency and capabilities framework; Fleming Fellowship Scheme.

### Surveillance System Strengthening

- Governance: support for AMR Coordination Committees & working groups; operational planning; cross-sectorial meetings and strategy reviews; evaluation(s).
- Quality assurance and control: site visits and audits, laboratory twinning / mentoring.
- Data: transfer and storage; safety and security; analysis software and training.
- Recurrent costs: utilities, maintenance of equipment, upkeep of laboratory space, small maintenance, personnel costs.

### Building Foundations for Surveillance Data Use

- Support to build demand for AMR data: general awareness among prescribers, dispensers and agricultural consumers (i.e. farm workers, agribusiness); publication charges; workforce training.
- Evidence based strategy, policy and practice change: data / information sharing conferences, meetings and initiatives; conference attendance; IT platforms for data sharing and awareness / transparency.

### Rational use of Antimicrobial Medicines

- AMU/C surveillance: development of strategies for AMU/C surveillance; use of AMU data for appropriate prescribing / informing stewardship programmes.

## Annex 2: Possible Fleming Fellowships in Laos

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic training	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Human	AMR Surveillance	DCDC	Analyse AMR surveillance data, understand data biases Keep up to date with all the available information on AMR and AMU in Lao PDR Understand the likely AMR mechanisms in Lao PDR	Contribute to designing future targeted AMR surveillance				Discuss AMR and AMU results from human and animals Present overall understanding of AMR in Lao PDR	<i>Combined with human and animal Laboratory and Surveillance Fellows</i> Salmonella typing and AST for stored Salmonella isolates – NCLE & NAHL
Human	Laboratory	NCLE			Culture, identification and AST Phenotypic testing for resistance (e.g. ESBL+)	Benchmark guidelines SOPs Quality control External quality assurance ISO accreditation – Preparatory activities		Discuss AMR and AMU results from humans and animals Present AMR results from humans (with Surveillance Fellow)	<i>Combined with human and animal Laboratory and Surveillance Fellows</i> Salmonella typing and AST for stored Salmonella isolates – NCLE & NAHL

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic training	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Human	AMR Surveillance	NCLE		Contribute to designing future targeted AMR surveillance			Collate and analyse existing AMR data (outbreak investigations) Analyse AMR surveillance data Understand data biases Interpret AMR results in consultation with microbiologist and AMU data	Discuss AMR and AMU results from human and animals Present AMR results from humans (with Lab Fellow)	<i>Combined with human and animal Laboratory and Surveillance Fellows</i> Salmonella typing and AST for stored Salmonella isolates – NCLE & NAHL
Human	AMU Surveillance	Setthathirath Hospital					Conduct survey of prescribing practices in 1 or a small group of hospitals Analyse and interpret AMU surveillance results Work with clinicians to modify prescribing practices to reduce potential for AMR	Discuss AMR and AMU results from human and animals Present AMU results from humans so that AMR results are related to AMU patterns	<i>Combined with human and animal Laboratory and AMR Surveillance Fellows</i> ? Link into Salmonella project – investigate AMU practices that may be associated with AMR patterns in Salmonella ? Recommend a change to prescribing practices in one area of a hospital and monitor changes in antibiotic use and impact on AMR
Animal	Laboratory	NAHL			Culture, identification and AST Phenotypic testing for resistance (ESBL+)	Benchtop guidelines Quality control ATCC strains External quality assurance		Discuss AMR and AMU results from human and animals Present AMR results from animals (with Surveillance Fellow)	<i>Combined with human and animal Laboratory and Surveillance Fellows</i> Salmonella serotyping and AST for stored Salmonella isolates – NAHL & NCLE

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic training	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Animal	AMR Surveillance	DVS		Contribute to designing future targeted AMR surveillance			Collate and analyse existing AMR data (clinical cases) Analyse AMR surveillance data Understand data biases Interpret AMR results in consultation with microbiologist and AMU data	Discuss AMR and AMU results from human and animals Present AMR results from animals (with Lab Fellow)	<i>Combined with human and animal Laboratory and Surveillance Fellows</i> Salmonella serotyping and AST for stored Salmonella isolates – NAHL & NCLE
Animal	AMU Surveillance	DVS					Design a survey in population, based on priorities as agreed with NAHL, DVS and OH technical subcommittee Separate and complementary to CIRAD study Analyse and interpret AMU surveillance results	Discuss AMR and AMU results from human and animals Present AMU results from animals	<i>Combined with human and animal Laboratory and AMR Surveillance Fellows</i> ? Link into Salmonella project Collect samples from a population of animals and people (based on results from AMR surveillance and AMU study)