

Terms of Reference

Second Fleming Fund Country Grant to Pakistan

1 Overview of this grant

This Fleming Fund Second Country Grant (CG2) for Pakistan will focus on progressing work carried out under the First Country Grant (CG1). It will focus on increasing federal and provincial level capacity and resources to oversee and implement AMR and AMU surveillance. In the human health sector, the grant will continue to support the national reference laboratory and will also strengthen AMR surveillance at 12 hospital sites across Pakistan. In the animal health sector two national reference laboratories will be supported and active surveillance will be continued and expanded. In addition, first steps will be taken towards institutionalising passive surveillance in animals.

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

The Grantee will need to ensure that inputs supported by the Fleming Fund align with those of other development partners.

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 15 months, ending no later than January 2022. Grant applications should be in the region of £5.5-6.5m, including capital, procurement, recurrent costs, and overheads and management costs but excluding key high cost items that will be procured centrally (automated blood culture instruments, automated AST platforms and MALDI TOF mass spectrometry instruments).

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 due to bacterial Antimicrobial Resistance, also known as 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 antimicrobial use, and prevention and control of infections in humans, animals, food, agriculture, and aquaculture sectors, are key to tackling AMR and call 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 antimicrobial-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 drug resistant infections. A Global Action Plan on Antimicrobial Resistance (GAP-AMR) has been developed by the World Health Organization (WHO), which acts as the blueprint for a multi-stakeholder global response to averting a global health crisis caused by AMR.¹

The Fleming Fund comprises a number of workstreams (see www.flemingfund.org for more information). 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 OH approach. Through funding to the Tripartite Alliance, the Fleming Fund has contributed to the development of National Action Plans (NAPs) 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 the Fleming Fellowship Scheme, as these will target capacity gaps identified in NAPs. The Fleming Fund also funds initiatives in academic institutions to develop guidance on the development of AMR surveillance systems such as the LSHTM Roadmap for developing an AMR surveillance system in human health systems (see Annex 2).

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 (DHSC) 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 and 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 bacterial infections, and to 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, including Pakistan. It can provide financial support up to 2022 to participating countries via three funding channels:

- Country Grants
- Fleming Fellowship Scheme Grants
- Regional Grants

The Fleming Fund is being independently evaluated by Itad, a specialist evaluation firm appointed by the DHSC for this purpose.

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

2.2 Problem statement to be addressed by the Fleming Fund

The main issues which are addressed by Fleming Fund Country Grants are outlined below (*please note*: these are general issues in LMICs with regard to AMR, and may not all be relevant in the case of Pakistan):

- There are too few microbiologists and laboratory technologists and even fewer with adequate training 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 Susceptibility Testing.
- There is no culture of surveillance for AMR in healthcare delivery
- There is little perceived use of surveillance data at any level
- 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 sustainable 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 there is 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 laboratory testing.
- There is a lack of understanding across all sectors on transmission patterns and drivers, such as inappropriate use of antimicrobial drugs.

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; and
- Promoting rational use of antimicrobial medicines.

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

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

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

- Increase in quality and quantity of AMR and AMU data collected;
- AMR and AMU data shared in country to support evidence-based policy and practice; and
- AMR and AMU data shared internationally to improve and inform the global response, in particular via the WHO GLASS programme for human health AMR data.

The Terms of Reference 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. In addition, the programme is also committed to evaluation, continued improvement and Value for Money (VfM). The Grantee is expected to demonstrate how they will align with these principles while implementing the grant.

- **Country Ownership:** The Fleming Fund Grants Programme works closely with Government of Pakistan (GoP) to ensure that activities undertaken through this grant are in line with Pakistan's National Action Plan on AMR (NAP). The Grantee is expected to plan and implement activities in close consultation with GoP, keeping country priorities and needs in mind, but within limits of the scope as mentioned in this Terms of Reference (ToR). Unless there are good reasons not to do so, Fleming Fund grants will chiefly invest in the public sector to support development of national public health systems.
- **One Health:** The Fleming Fund recognises that the problem of AMR is a great danger to human health and cannot be controlled without a OH approach. A specific set of OH investment parameters has also been developed and are summarised below. This approach is aligned with key documents and guidelines from OIE² and FAO³ 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, AMU and AMC surveillance in all sectors.

Applicants should explicitly propose activities in the application to demonstrate how they will achieve the above.

- **Alignment of Approach:** The Fleming Fund Grants Programme seeks to invest in areas which complement and build on work done to date. Grant applicants will need to demonstrate that

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

³ The FAO Action Plan on Antimicrobial Resistance, 2016-2020.

they understand GoP investments and 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, applicants will need to demonstrate how their proposals add value to existing and planned investments and systems.

- **Sustainability:** The Fleming Fund Grants Programme focuses assistance on national systems with a view to long-term sustainability. Investment size and scope are as far as possible, aligned with national government spending so that systems created with Fleming Fund grants are sustainable within the public health system. Applicants should explain how they will undertake actions to achieve sustainability on a long-term basis.

2.5 Fleming Fellowship Scheme

The Fleming Fellowship Scheme is part of the broader Fleming Fund Grants Programme and is managed by Mott MacDonald. Fellowships provide funding to support on-the-job training over an 18- to 24-month programme of structured learning, mentoring and skills development for four to eight Fellows in each investment country. The Fellowships do not duplicate basic training, rather they focus on building advanced skills and leadership to promote the application of best practice in identified 'Beneficiary Institutions', while promoting the One Health principle. Beneficiary Institutions are organisations such as AMR reference laboratories national epidemiology units in the human and animal health sectors, hospitals and/or national drug administration agencies that add strategic value and complementarity to achieve the Fleming Fund's aims in the country. They are also institutions most likely to derive sustainable benefit from the Fellowship activities and many are supported through the Country Grant.

The initial focus of the Professional Fellowship Scheme is on strengthening the quality of laboratory diagnostic data and the analysis and use of AMR and AMU surveillance data in Beneficiary Institutions. Fellows in each country are supported by external mentors from world class institutions who provide the expertise required to support the needs of the Fellows as well as to help them to improve the sustainability of AMR programmes in their institution. The data they generate will be applied to deliver evidence-based approaches to tackling AMR, for example to improve antimicrobial stewardship.

In Pakistan there are currently six professional Fellows. Fellows are undertaking a variety of activities including data collection and analysis, developing tools, protocols and SOPs and receiving training. They are also carrying out collaborative projects. The workplans for the current Fellows are attached at Annex 3. Recruitment of a further cohort of professional Fellows, including clinician Fellows, is planned for October 2020.

Policy Fellowships will also be selected for Pakistan in October 2020, with preparation work taking place beforehand. The Fellowships will provide professional development of two individuals with the right qualities from multiple disciplines to enable them to strategically advance Pakistan's AMR policy / One Health priorities. The Fellowships will have the following objectives:

1. Supporting the national AMR Coordination Committee by promoting strong leadership and vision for the delivery of AMR National Action Plans.
2. Raising awareness of AMR within national leadership by providing information on the causes and implications of AMR, options for control and prioritisation of robust AMR responses.

3. Promoting evidence-based policy development by supporting evidence reviews, cross sectoral collaboration and inclusive stakeholder engagement.
4. Strengthening communities of practice among Fleming Fellows by supporting participation of fellows in evidence-based decision-making and national AMR guidance mechanisms.

The grantee will be expected to ensure coherence and alignment between the activities on the country grant and those of all the Fellows, throughout the life of the grant. The grantee is expected to:

- Ensure that Fellows are aware of country grant activities relevant for their own work plans, for example by including them in stakeholder consultations.
- Avoid duplication. The country grant should not be covering work that Fellows are doing, and vice versa.
- Ensure synergies are maximised, for example by disseminating SOPs developed by the Fellows.
- Work together with Fellows where appropriate e.g. data gathering, transporting samples, but should avoid interdependency.
- Ensure that any training provided to the Fellows aligns with that provided by the mentors from the Fellowship scheme Host Institutions.
- Ensure that the Host Institutions are aware of training being provided by the grantee

2.6 Fleming Fund Regional Grants

Pakistan is currently involved in five Regional Grants. Regional grants are expected to align with country grants and find synergies between them. Similarly, country grantees who are planning inputs are expected to ensure their work does not duplicate that of the regional Grants.

AMR/AMU retrospective data collection, analysis and dissemination

This grant aims to expand the volume of historical and current human health data on AMR and antimicrobial usage. In many low- and middle-income countries, institutions (academic, research, medical, etc) have been collecting AMR data for many years but have not shared this information publicly. By partnering alongside these institutions to collect and digitise existing data, grantees will help establish an AMR baseline across Fleming Fund priority countries.

Grantees have been tasked with developing a plan for AMR and antimicrobial usage data collection, rating the quality of the data collected and retrieving the information. Information related to microbiology, clinical practice and epidemiology, antimicrobial consumption and whole genome sequencing will be collected.

External Quality Assessment

This grant maps coverage, availability and uptake of EQA programmes in human and animal health laboratories. Barriers to participating in existing EQA programmes are being identified, and the grantee is exploring the risks and benefits of establishing formal regional EQA systems (e.g. biosecurity, data ownership, sample shipping) to complement existing international schemes, as these may be difficult for some countries to access. The grantee will then strengthen or help establish EQA Reference Centres. This will include formalising collaboration with all Fleming Fund Country Grants for establishment of a) quality assured identification of isolates and b) appropriate logistics for effective movement of isolates.

Common surveillance protocols

This grant focuses on standardising the collection and analysis of data by developing common protocols. For data to be comparable, it must be collected in the same way. This is particularly challenging within animal health, aquaculture, environmental and food safety surveillance, as there are no international guidelines pertaining to AMR data collection.

The grantee has been tasked with identifying the most critical data protocols needed in either animal health, aquaculture or environmental sectors and then developing them. They will also support the roll-out of the Tricycle Protocol in some Fleming Fund priority countries.

Microbiology training; epidemiology training

Under this grant quality microbiology and epidemiology training is being delivered to laboratory and surveillance staff from national reference laboratories (human, animal and environmental health). This includes laboratory and data management and advanced laboratory skills.

Training in AMR epidemiology and surveillance methods will be provided for human, animal and environmental health laboratories and/or national coordination centres for AMR (e.g. AMR Coordination Committee or Technical Working Group(s)).

Improving data analysis and sharing

This grant provides support to regional bodies for data sharing and policy-relevant analysis for both human and animal health. The grantee is working with the regional bodies to identify policy bottlenecks around data sharing for regional analysis, and to assess which approaches to data collection and analysis would be most beneficial for policy discussions. Regional plans will be developed to improve data sharing and analysis and to identify an optimal number of reference laboratories to obtain quality data to inform regional analysis.

3 Scope of grant

3.1 Duration and phasing of the grant

The grant is expected to start by November 2020, and will last for approximately 15 months, ending no later than January 2022. The table in Section 3.3 illustrates which objectives and outputs are expected to be delivered in which phase.

3.2 Unfinished business from the existing Country Grant

The Objectives and Outputs below are based on results from the existing Country Grant (CG1) being fully achieved. Objectives and outputs from the RfP for CG1 are attached at Annex 4 for reference. Any key outstanding issues which were not in the final workplan for CG1 or which will not be achieved by the end of CG1, should be included in CG2.

3.3 Grant Objectives and Outputs

The objectives and outputs for this Country Grant are summarised as follows, with more detail provided in Section 4. It is expected that applicants will respond to the ToRs by developing and proposing activities that are costed, accompanied by appropriate indicators (see Section 6). All

inputs must be permitted under the list of Eligible Funding Items, as outlined in Section 8 and Annex 6.

For human health, the Country Grant is intended to support and improve implementation of the WHO GLASS programme and Grantees should refer to the roadmap for GLASS participation produced by the London School of Hygiene and Tropical Medicine (Annex 2). Please note Annex 1 which is a table of functionalities for laboratories based on that LSHTM roadmap. Grantees will recognise these functionalities from the site reports in the quarterly monitoring form.

Table 1: Grant objectives and outputs

| Objective/Output |
|---|
| Objective 1: Strengthen capacity and resources towards sustainability of efforts on AMR and AMU surveillance |
| Output 1.1: Functional One Health governance and coordination for AMR and AMU surveillance established and sustained at federal level |
| Output 1.2: Functional One Health governance and coordination for AMR and AMU surveillance initiated within 2 provinces. |
| Output 1.3: Functional One Health coordination and data sharing for AMR and AMU surveillance initiated between federal and provincial levels |
| Output 1.4: One Health surveillance of AMU and AMC progressed |
| Objective 2: Sustain existing services and expand AMR surveillance in the human health sector |
| Output 2.1: The National Institute of Health has the capacity to function as the national reference laboratory for human health |
| Output 2.2: NIH has the capacity to oversee the implementation of the national AMR surveillance strategy for human health |
| Output 2.3: Strengthened AMR surveillance at 12 surveillance sites. |
| Output 2.4: Greater clinical engagement |
| Output 2.5: The private sector shares AMR data |
| Objective 3: Sustain existing services and expand AMR surveillance in the animal health sector |
| Output 3.1: Improved capacity of NVL and NRLPD to function as national reference laboratories for animal health |
| Output 3.2: Implementation of active surveillance progressed |
| Output 3.3: Selected provincial peripheral laboratories participate effectively in the national surveillance effort |
| Output 3.4: Passive surveillance initiated |

3.4 Selected laboratories

24 human and animal surveillance site laboratories have been identified as priority sites to be supported by CG2 (Table 2). The grantee has assessed all these sites.

Table 2: Proposed surveillance sites

| Name | Role | Location | Sector |
|--|-------------------|--------------------|--------|
| National Institute of Health | AMR NRL | Islamabad | Human |
| Abbas Inst. of Med. Sci, Azad Jammu & Kashmir | Surveillance site | Kashmir | Human |
| District Headquarter Hospital, Gilgit | Surveillance site | Gilgit-Baltistan | Human |
| Dr Ruth K.M. Pfau (Civil) Hospital | Surveillance site | Sindh | Human |
| Jinnah Postgraduate Medical Centre, Karachi | Surveillance site | Sindh | Human |
| Mayo/ King Edward Hospital, Lahore | Surveillance site | Punjab | Human |
| Shaukat Khanum Memorial Cancer Hosp., Lahore | Surveillance site | Punjab | Human |
| Sheikh Zayed Hospital, Lahore | Surveillance site | Punjab | Human |
| Nishtar Medical University, Multan | Surveillance site | Punjab | Human |
| Armed Forces Institute of Pathology, Rawalpindi | Surveillance site | Punjab | Human |
| Hayatabad Medical Complex, Peshawar | Surveillance site | Khyber Pakhtunkhwa | Human |
| Khyber Teaching Hospital, Peshawar | Surveillance site | Khyber Pakhtunkhwa | Human |
| Bolan Medical Complex, Quetta | Surveillance site | Baluchistan | Human |
| National Veterinary Laboratory | AMR NRL | Islamabad | Animal |
| National Reference Laboratory for Poultry Diseases | AMR NRL | Islamabad | Animal |
| Disease Diagnostic Laboratory, Gilgit | Surveillance site | Gilgit-Baltistan | Animal |
| Poultry Research Institute, Karachi | Surveillance site | Sindh | Animal |
| Central Veterinary Diagnostic Laboratory, Tando Jam | Surveillance site | Sindh | Animal |
| Provincial Disease Diagnostic Laboratory, Lahore | Surveillance site | Punjab | Animal |
| Poultry Research Institute, Rawalpindi | Surveillance site | Punjab | Animal |
| Disease Investigation Laboratory, Peshawar | Surveillance site | Khyber Pakhtunkhwa | Animal |
| Poultry Research Institute, Mansehra | Surveillance site | Khyber Pakhtunkhwa | Animal |
| Disease Diagnostic Laboratory, Muzaffarabad | Surveillance site | Kashmir | Animal |
| Disease Investigation Laboratory, Quetta | Surveillance site | Baluchistan | Animal |

4 Objectives and potential priorities for the second country grant

4.1 Objective 1: Strengthen capacity and resources towards sustainability of efforts on AMR and AMU surveillance

Effective implementation of AMR and AMU surveillance in Pakistan will depend on improved clarity of roles and responsibilities at federal and provincial levels, better coordination between those levels and improved understanding and capacity in the provinces. This objective therefore focusses on progressing the groundwork completed by the grantee under CG1 on (i) identifying roles, responsibilities and coordination mechanisms under a OH multi-tier AMR coordination mechanism and (ii) costing the federal level implementation of the NAP.

Output 1.1: Functional One Health governance and coordination for AMR and AMU surveillance established and sustained at federal level

A National AMR Multisectoral Steering Committee has been formed under the leadership of MoNHSR&C, consisting of federal and provincial health, livestock and environment sectors, plus international partners, professional associations and regulatory bodies. It is chaired by the Secretary of Health. As such it has the potential to mobilise political support across both federal and provincial levels. It is mandated to meet annually, and terms of reference have been agreed.

The grantee should propose how the Fleming Fund could support more effective functioning of this committee.

An AMR Secretariat has been proposed as a One Health coordination hub for all activities related to the AMR NAP. Outline terms of reference, yet to be agreed, include forming a committee of multisectoral stakeholders to support a One Health approach, establishing the AMR surveillance system, overseeing AMR surveillance implementation at both national and provincial levels against key performance indicators, including quality assurance, ensuring information sharing, and convening federal – provincial dialogue. In addition, it will act as the central data repository carrying out data management and aggregating and analysing multisectoral AMR surveillance data. Based in NIH it will report to MoNHSR&C, and membership is expected to include technical experts and stakeholders. The mandate of the Secretariat is wider than that of the Fleming Fund: for example, it will develop a national public health research agenda and promote engagement of civil society and patient groups in improving practices in infection prevention and control. Inclusion of veterinary and environmental health expertise in the AMR secretariat can help to ensure that a 'One Health' approach is embedded. For improving coordination within the Animal Health sector, a coordination unit should be established in the MoNFSR that can liaise and coordinate with the provincial livestock departments.

A PC1 has been approved for government support for the Secretariat but transfer of funds has been delayed by COVID-19. The grantee should therefore consider how the Fleming Fund can support the start-up and functioning of the One Health aspects of the Secretariat in the interim, in line with the Fleming Fund mandate. This could include developing a long-term support plan and providing limited HR support until regular NIH staff can be recruited.

The grantee should also help to establish the Technical Working Groups which are most closely aligned with FF priorities. The TWGs to be supported might include (but not be limited to) Awareness and Advocacy, housed in MNHSR&C (to facilitate use of data for policy-making); AMR

surveillance, housed in NIH; and Antimicrobial Stewardship (AMS), housed in DRAP or with MNHSR&C (to facilitate implementation of the AMU/C strategy and better clinical engagement). The grantee will be expected to assist by supporting nominations and where possible, helping them to develop and start to implement their terms of reference.

Other federal level coordination mechanisms have been proposed (and some are in place in some form) to address the issue of coordination within and between sectors. These include a National AMR Laboratory Working Group, a Sub-Federal AMR Laboratory Working Group, a Human Health Coordination Committee, an Animal Health Coordination Committee, and a Technical One Health Laboratory Working Group. Terms of reference have yet to be finalised and agreed. Focal points have been identified but their responsibilities have not yet been incorporated into their job descriptions.

The grantee is required to support the National Laboratory Working Groups in human and animal health, aligning inputs with other development partners who may also be providing inputs.

Support by the grantee could include meeting facilitation, technical knowledge, initial work in data driven policy design (if feasible), advocacy strengthening and project coordination capacity. Inputs should be in line with the Fleming Fund mandate⁴, aligned with any other support being provided by GoP and other sources, and based on a clear needs and capacity assessment of federal level government.

The grantee should also help the federal level focal points better fulfil their ToRs.

The implementation of Tricycle is a valuable way to promote integrated One Health surveillance. Pakistan has piloted Tricycle and is expected to be involved in piloting and contributing to the development of TRIuMPH. In the interim, the grantee is requested to explore how further rounds of Tricycle in different locations, using Pakistan's whole genome sequencing (WGS) capacity, could be usefully implemented under CG2. This may also be an opportunity for joint integrated surveillance pilot studies with some provinces (see also output 1.3).

Note: the Fleming Fund does not anticipate the need for environmental samples taken under Tricycle to be processed in a dedicated EH laboratory, if capacity is lacking in that sector. Rather one of the animal reference laboratories should be engaged, with expert inputs to develop SOPs and to train on the specific methods required for organism isolation.

Other strategies to be considered by the grantee could include:

- Sensitising senior government officials to AMR surveillance, across sectors and ministries, e.g. finance.
- Supporting the implementation of the new federal investment in AMR surveillance in human health, currently the subject of a PC-1.
- Supporting the development of an investment case (PC-1) for animal health AMR surveillance.
- Supporting the development of an investment case (PC-1) for development of Provincial Action Plans for AMR.
- Identifying key positions in the AMR surveillance system (AH and HH) and providing advocacy to ensure those key positions are filled and remain filled.
- Continuing support to the AMR Secretariat if approval of the PC-1 is delayed.

⁴ Insert a couple of lines about FF mandate.

- Establishment of AMR coordinating units at MoNFSR and if possible MoCC.
- Providing technical assistance to federal government to review or draft regulations or legislation on AMR and antimicrobial use in various sectors as necessary.

Deliverables:

- NIH plans and hosts one meeting of the National AMR Steering Committee.
- One key representative for the Steering Committee is nominated from each of the relevant ministries at federal and provincial levels.
- The National AMR Steering Committee has improved functionality.
- AMR Secretariat is functional and:
 - identifies focal points at provincial level
 - includes representation from the Animal Health Sector
 - re-activates the AMR Steering Committee (coordinates meetings/correspondence (virtual or onsite))
 - Continues reporting on a quarterly basis via AMR Newsletter that presents analysis of AMR Surveillance data
- Priority Technical Working Groups are identified and established as sub-committees of the National AMR Steering Committee
- Coordination unit is established within the MoNFSR's AHC office to coordinate with provincial livestock departments and relevant AH ministries
- National AMR Laboratory Working Groups in both Human and Animal Health are reactivated.
- The AMR Lab Working Group in Animal Health drafts policy and guidelines for testing in veterinary/poultry sector e.g. sampling, reporting etc., that can be applied in both public and commercial labs.
- AMR dashboard for data sharing developed and implemented, and the AMR secretariat supported to manage it effectively.
- Technical support provided to HH and AH sectors for developing mechanisms to enable government funding in AMR at provincial level (e.g. PC1s).
- Provincial Action Plans for AMR progressed.
- Advocacy sessions carried out with policy makers and target audience at national and provincial levels.
- Further round(s) of Tricycle carried out (in coordination with the TRIuMPH team), or elements of Tricycle included in the AH AMR surveillance pilot.

Output 1.2: Functional One Health governance and coordination for AMR and AMU surveillance initiated within 2 provinces.

The provinces have a key role to play in carrying out and reporting on AMR surveillance as part of the national system. Provincial level AMR surveillance data should also be used to influence provincial level policy and practice. Their autonomy means that each one needs to have the commitment and capacity to own, lead, resource and deliver AMR surveillance efforts. However, their technical and resource capacity to do so is currently very limited.

Under the second country grant the grantee should identify 2 provinces and support them to take the first steps in tackling AMR surveillance.

Strategies could include:

- Building high level political support to address AMR, especially at chief minister level.
- Building stakeholder understanding of AMR surveillance.
- Developing costed provincial AMR action plans.
- Carrying out political economy analyses to inform grant strategies and activities.
- Supporting advocacy for human and financial resource allocation e.g. by generating data to influence investment cases.
- Identifying key positions in the AMR surveillance system (HH and AH) and providing advocacy to ensure those key positions are filled and remain filled.
- Providing technical assistance to provincial governments to draft regulations or legislation on AMR surveillance and antimicrobial use.
- Supporting provinces to develop and implement functional One Health coordination mechanisms. This could include the formation of provincial multisectoral AMR coordination committees and supporting coordination and cooperation between laboratories.
- Supporting the work of AMR focal persons in the human, livestock and poultry sectors by helping to clarify their job descriptions and mandates and providing some support for implementation of their roles.
- Holding information sharing events – see Priority 1.3.

Deliverables, provisionally focused on Sindh and KP, subject to their agreement:

- Selection of provinces agreed with provincial health secretaries and director generals.
- Political Economy Analysis for AMR/AMC and AMU surveillance carried out at provincial level.
- Incorporation of AMR dashboards into existing IT platforms at provincial level progressed e.g. IDSR surveillance DHIS 2 and Integrated M&E system potentially integrated with WHONET; possible expanded partnership with AusVet or with DAI's Center for Digital Acceleration.
- IDSR coordination units/personnel leveraged to set up provincial AMR units under a 'One Health' approach.
- Legislative environment analysed for regulating antimicrobial use at provincial level.

Output 1.3: Functional One Health coordination and data sharing for AMR and AMU surveillance initiated between federal and provincial levels

Coordination between federal and provincial level governments is a particular challenge in Pakistan and likely to remain so due to the 18th constitutional amendment, which gave considerable autonomy to the provincial governments and led to the development of unclear relationships between the two levels. However, better coordination between the two tiers is vital for the effective implementation of the national AMR surveillance system. Coordination across provinces is also important.

Currently the only effective platform for coordination between respective federal ministries and provincial departments is the National AMR Multisectoral Steering Committee. In addition, no formal coordination mechanism exists between the federal human health, livestock and poultry laboratories and their respective counterpart provincial laboratories. Interaction is infrequent and needs-based.

The grantee should consider ways of facilitating coordination and accountability pathways between the different tiers, including helping to institutionalise the coordination mechanisms proposed in October 2019⁵.

The grantee should also consider how it can help to strengthen the relationship between the AMR Secretariat and the provinces, for example by facilitating agreements on data sharing.

The grantee should also propose ways in which coordination between provinces could be supported.

Under CG1, two information sharing events were planned to disseminate AMR and AMU findings to policymakers, media, and industry. We propose that these events (or variations on them to take account of COVID) be continued under CG2 to build political commitment to AMR at, and between, federal and provincial levels. The events could inform and sensitise stakeholders on the importance of One Health multisectoral federal and provincial coordination in combatting AMR, the value of AMR and AMU data, and the need for continued resource allocation.

The grantee is invited to propose the scope and frequency of these events, which could take place at both federal and provincial levels.

The grantee is also asked to consider other options for progressing coordination between the two levels, building on the work started under CG1.

Deliverables, provisionally focused on Sindh and KP, subject to their agreement:

- Formal AMR data sharing agreements made between identified provincial AMR coordinating units and federal AMR secretariat, Sindh, KP and GB/AJK. Data sharing could include establishing and notification of coordinating mechanisms, agreement with federal counterparts on reporting and information sharing, including provincial reports/chapters in the AMR newsletter, and progress review meetings with provincial counterparts.
- TA provided to assess and develop an implementation plan for provincial level analysis of AMR and AMU data (see also objective 1.2 including data sharing agreement with federal level)
- COVID appropriate AMR information sharing events carried out at, and led by, provinces.
- Potential for AMR dashboards at Provincial level explored.
- Communication materials developed and activities carried out for point of sale pharmacies. Orientation sessions carried out, in coordination with the Provincial Drug Control Administrations/Authorities

Output 1.4: One Health surveillance of AMU and AMC progressed

The original plans for CG1 (see CG1 outputs 3.3 and 4.3) have had to be adjusted to align with other partners' activities and address government priorities.

Agreement has been reached that the Fleming Fund will contribute to expansion of the WHO led Point Prevalence Survey, including surveillance sites to be supported by the Fleming Fund. The grantee will also work with OIE to implement a PPS in the animal health sector. Both these PPSs should be completed by the end of CG1.

A technical working group has been proposed with technical partners and representatives of DRAP, MoH, NIH and MoNFSR. This is expected to develop a two-year work plan for improving AMC/AMU

⁵ One Health coordination mechanism for antimicrobial resistance containment, H. Qureshi, October 2019

data collection and analysis, map out areas of possible future support, and plan capacity development in DRAP and elsewhere.

A workshop, supported by the grantee, has started the process of stakeholder consultation on assessing AMC in the animal health sector. There has also been an initial mapping of sources of antimicrobials used in animals.

The grantee is invited to propose further steps towards promoting a One Health approach to AMU and AMC surveillance under CG2, in line with federal and provincial priorities.

Strategies could include:

- Supporting further rounds of PPS in the human health sector.
- Supporting PPS follow-on work in surveillance sites and at provincial level e.g. working with the AMR or stewardship committee to develop an ongoing audit and intervention programme to improve use of antimicrobials.
- In animal health, using the results from the PPS as a pilot, to decide whether and how to scale up further rounds of PPS for example by covering different species or geographical areas.
- Using results to inform policies and regulations.
- Steps towards a greater One Health emphasis on developing AMU and AMC activities.
- Working with the proposed Animal Health coordination office within MoNFSR (see Objective 1, Output 1.1) to facilitate reporting of AMU data to OIE

Deliverables, provisionally focused on Sindh and KP, subject to their agreement:

- Point Prevalence Survey carried out at provincial levels
- Results from the PPSs inform provincial departments and DCAs on AMU and AMC and where possible, feed into options for improving oversight of the DCA
- Further PPS in AH carried out, by extending the scope to a different production system, e.g. aquaculture, and/or different agroecological zone.
- KAP assessment carried out of veterinary drug prescribers for food animals to understand gaps in knowledge and barriers to best practice.
- Findings from the KAP feed into policy level discussion at national and provincial levels to inform:
 - communications to end-users on anti-microbial use
 - policy makers on regulating use of antimicrobials
- AHC/MoNFSR supported to report data to OIE.
- KAP assessment carried out of farmers/producers related to antimicrobial use, farm biosecurity and animal husbandry for gaps in knowledge and barriers to best practice, and findings used to inform changes in practice and/or stewardship programme implementation.

4.2 Objective 2: Sustain existing services and expand AMR surveillance in the human health sector

Output 2.1: The National Institute of Health has the capacity to function as the national reference laboratory for human health

An assessment carried out in October 2019 reported that the NIH laboratory had the following strengths - the quantity and qualifications of its staff, access to a range of automated phenotypic typing systems (Vitek and MALDI-ToF systems), adequate consumables and reagents, the existence of an LMIS which reports into WHONET, and ISO9001 certification. A number of areas were identified for improvement, including SOPs, quality checks, biosafety, workflow, some equipment gaps and implementation of the EQA.

Based on those assessments, laboratory renovations have begun, and equipment is being purchased. NIH is also receiving support and investment focussed on attaining ISO 15189, and strengthening its EQA programme.

Further capacity building and equipment provision can take place under CG2 but needs to be planned in line with the proposed government investment. NIH has applied for a GOP PC1 grant for AMR worth PKR350 million (~US\$2.1m), which will have a significant impact on the development of AMR surveillance at NIH. Fleming Fund investments are expected to be aligned with national resources, should not displace them and should avoid duplication. The scale and scope of support to NIH by the Fleming Fund under CG2 will be dependent on the timing of the PC1 grant decision, what it will cover and when funding will be released.

Assuming Fleming Fund support is needed for CG2, the grantee should ensure that by the end of the grant NIH has the capacity to perform the specified 'core' functions for reference laboratories (see Annex 1). Some additional functions are also required, as below. Progress will be monitored on a quarterly basis.

Our expectation is that by the end of the grant, in addition to the core functions, NIH will be able to perform:

- confirmatory testing for referring surveillance sites: organism ID, resistance mechanism, (e.g. identify ESBL producers, CREs, MRSA)
- QC – checking 10% of isolates from sentinel sites for correct ID and AST results with supporting corrective measures if performing poorly.

The grantee will be required to prioritise attainment and retention of biosafety level 2 (BSL-2). This should be verified by independent assessment with the cost of the assessment included in the Country Grant.

The grantee will be required to arrange and pay for maintenance contracts for the Vitek and MALDI-ToF in NIH for up to 5 years if there is no government funding for them. If not covered by CG1 these costs will be factored into the final grant amount and the Grantee is expected to facilitate the process of setting up the contract, and work with the suppliers and government to finalise the agreements.

The grantee will be expected to ensure a reliable and regular supply of consumables and reagents to meet the expected throughput of samples collected through passive surveillance. These should be included in the grant budget. If it is necessary to purchase these outside the usual system, the

grantee should nevertheless work with the laboratory to develop reliable stock management and procurement processes to minimise future stock outs.

In addition to supporting the functionalities stated in Annex 1, the grantee can continue to provide technical assistance and resources to support NIH's participation in the external quality assurance scheme. Similarly, other extended or advanced functions can be considered for Pakistan if the grantee is able to provide sufficient justification.

The grantee should also support the setup of a biorepository, which by the end of the second country grant should consist of a secure -80° freezer (or alternatively, a lyophilization system), a database, and SOPs for storage, access and use. The complexity should be related to the expected number of isolates to be stored: if the repository is a single freezer, a Microsoft Excel spreadsheet to log isolate position and number will be adequate.

The grantee will also need to support implementation of WHONET at NIH, or, if a functioning LIMS is in place, should ensure that data can be exported in a WHONET compatible format to facilitate national collation and GLASS reporting.

The grantee should also include within their budget the cost of laboratory assessments at the end of the grant, to measure progress from the initial assessments.

Deliverables:

- NIH performs the specified 'core' functions for reference laboratories (see Annex 1)
- NIH performs confirmatory testing for referring surveillance sites: organism ID, resistance mechanism, (e.g. identify ESBL producers, CREs, MRSA, MIC testing for borderline isolates)
- NIH performs QC for sentinel sites – checking 10% of isolates for correct ID and AST results with corrective measures if performing poorly.
- NIH achieves and retains biosafety level 2 (BSL-2).
- There is a reliable and regular supply of consumables and reagents to meet the expected throughput of samples.
- NIH continues its enrolment in an International EQA and achieves acceptable scores.
- A functional biorepository is in place.
- NIH makes progress towards / achieves / retains ISO 15189.
- 5-year service contracts are in place for MALDI-ToF and Vitek (if necessary due to lack of Government funding).

Output 2.2: NIH has the capacity to oversee the implementation of the national AMR surveillance strategy for human health

In its capacity as AMR Secretariat, and in addition to its functions as the national reference laboratory, NIH is charged with coordinating the implementation of the human health surveillance system. This will include overseeing data management and reporting, coordinating data submission to GLASS, monitoring and evaluation, coordinating AMR workshops and training, providing mentorship for surveillance sites and coordinating surveillance site data transmission and sample or isolate transport from the surveillance sites.

The grantee is invited to propose how it can support the development of NIH in this role during CG2.

Deliverables:

- The sentinel site network is expanded to include additional sites.
- NIH staff effectively oversee improved reporting (timeliness and correctness) by the sentinel sites.
- NIH can provide support for WHONET use and troubleshooting at sentinel sites.
- NIH carries out step down training on AMR laboratory technologies with provincial and district sentinel labs.
- NIH makes progress towards achieving ISO 17043 accreditation for provision of proficiency testing.
- NIH team carries out supervisory visits to sentinel sites.
- Mechanism established for sharing isolates/samples between the NRLs.

Output 2.3: Strengthened AMR surveillance at 12 surveillance sites.

Country Grant 1 focused on strengthening the reference laboratory. Country Grant 2 provides the opportunity to develop the wider surveillance system, in line with the draft surveillance strategy.

Twelve potential surveillance sites have been assessed with a view to providing Fleming Fund support. The assessments indicated that the labs currently have some capacity, but many aspects require strengthening – see Table 3.

Of the 12, six have previously reported into GLASS. The priority for CG2 is to improve the quality and quantity of their reporting, and to bring the other six laboratories into the national surveillance network, enabling them to provide data to GLASS as well.

Table 3: Overview of Human Health Laboratories by Region

| | | GLASS entry 2018-19 | Capacity ⁶ | | | | | Average number of specimens processed per month ⁷ | | | | |
|---------------------------|---|---------------------|-----------------------|---------------|--------|------------|--------|--|-------|-------|-----------------------|----------------|
| | | | Blood Culture | Infra-struct. | Media | ID and AST | QMS | Blood | Urine | Stool | Genit. swabs for STIs | AST |
| Kashmir | Abbas Inst. of Med. Sci, Azad Jammu & Kashmir | | Orange | Green | Red | Green | Red | 90 | 250 | 100 | 50 | 500 |
| Gilgit-Baltistan | District Headquarter Hospital, Gilgit | | Red | Orange | Red | Red | Red | 0 | 0 | 0 | 0 | 0 |
| Sindh | Dr Ruth K.M. Pfau (Civil) Hospital | Y | Orange | Green | Orange | Green | Orange | 1,000 | 700 | 6,000 | 0 | 3,600 |
| | Jinnah Postgraduate Medical Centre, Karachi | Y | Orange | Orange | Orange | Orange | Orange | 1,000 | 2,500 | 60 | 0 | 2,000 |
| Punjab | Mayo/ King Edward Hospital, Lahore | Y | Orange | Orange | Orange | Orange | Red | 700 | 550 | 0 | 20 | 600 |
| | Shaukat Khanum Memorial Cancer Hosp., Lahore | Y | Orange | Orange | Orange | Green | Orange | 4,000 | 2,300 | 1,000 | 100 | 950 |
| | Sheikh Zayed Hospital, Lahore | Y | Orange | Orange | Orange | Orange | Orange | 3,000 | 1,500 | 30 | 0 | 1,500 |
| | Nishtar Medical University, Multan | | Orange | Orange | Orange | Green | Orange | 100 | 300 | 15 | 200 | 300 |
| | Armed Forces Institute of Pathology, Rawalpindi | Y | Orange | Green | Green | Green | Green | 500 | 9,000 | 2,100 | 250 | - ⁸ |
| Khyber Pakhtunkhwa | Hayatabad Medical Complex, Peshawar | | Orange | Orange | Orange | Orange | Red | 300 | 600 | 80 | 0 | 800 |
| | Khyber Teaching Hospital, Peshawar | | Orange | Red | Red | Orange | Red | 600 | 1,000 | 20 | 0 | 800 |
| Baluchistan | Bolan Medical Complex, Quetta | | Orange | Red | Red | Orange | Red | 60 | 60 | 60 | 0 | 60 |

Key: **Green** - no support required; **orange** - some capacity which requires strengthening; **red** – no or extremely limited capacity.

⁶ Data source: AMR Sentinel Sites Readiness Assessment, R. Dacombe, January 2020

⁷ Data source: Laboratory assessments, October 2019

⁸ Not known

Capacity development plans for the laboratories are being developed and implemented for the remainder of CG1 and include basic functions of sample collection, handling and transportation, and bacterial isolation and identification. Some laboratories will also receive training in higher-level functions such as biosafety, biosecurity, molecular diagnostics, and LQMS. Procurement of equipment is underway.

The laboratory assessments carried out in October 2019 identified that organisation and general management of the laboratories will also need to be addressed. The assessors also recommended that improvement in capacity could only be achieved through ‘consistent, sustained support over a period of time’ which ideally should ‘include a mentorship-based approach rather than training alone.’⁹

By the end of this second country grant each laboratory should have made clear progress towards sustainable capacity to perform blood cultures, and bacterial ID and AST for the GLASS priority pathogens expected in blood (*E.coli*, *Klebsiella* spp., *Acinetobacter* spp., *Salmonella*, *Streptococcus pneumoniae*, and *S. aureus*). Of note, in the 2018/2019 GLASS report, none of the Pakistan laboratories was able to provide data on *S. pneumoniae*. Ability to culture, identify and perform AST on *S. pneumoniae* from blood cultures should therefore be a priority in CG2.

More widely, the grantee should ensure that each surveillance site has progressed towards achieving the specified ‘core’ functions by the end of the grant (see Annex 1), prioritising activities that will achieve that. Progress at each site will be monitored on a quarterly basis. Progress beyond ‘core’ is not necessary for sentinel site laboratories but may be part of the grant if considered appropriate. For example, busy hospital laboratories processing large numbers of samples could be considered for support to progress to ‘advanced’ or ‘extended’ functions and should be supported to maintain these functions if already achieved.

The grantee will be expected to support the surveillance sites to develop systems to integrate clinical and laboratory data so that basic demographic and clinical data (e.g. age, gender, clinical syndrome etc) can be matched with samples and isolates: as a minimum, isolates and laboratory data should be stored using unique alpha-numeric identifiers which can be linked back to the source patient. Data should be shared with the National AMR Secretariat.

The grantee will also need to support implementation of WHONET at the surveillance sites, or, if a functioning LIMS is in place, to ensure that data can be exported in a WHONET-compatible format to facilitate national collation and GLASS reporting.

The grantee will be required to prioritise attainment and retention of biosafety level 2 (BSL-2) for all sites. This should be verified by independent assessment, with the cost of the assessment included in the Country Grant.

The grantee should also include within their budget the cost of laboratory assessments at the end of the grant, to measure progress from the initial assessments.

Deliverables:

- Agreement reached with provinces about how to structure their AMR surveillance networks.
- At least one major sentinel laboratory in each province/area is identified (and agreed with by their respective provinces) as a potential “regional/provincial AMR reference laboratory”.

⁹ Ibid, p.4.

- Regional/provincial AMR reference laboratories are refurbished and achieve 'core' functions by the end of the grant (see Annex 1).
- Peripheral laboratories have made clear progress towards achieving the specified 'core' functions by the end of the grant (see Annex 1).
- All laboratories, including the peripheral laboratories, have made clear progress towards sustainable capacity to perform blood cultures, bacterial ID and AST for the GLASS priority pathogens expected in blood (*E. coli*, *Klebsiella* spp., *Acinetobacter* spp., *Salmonella*, *Streptococcus pneumoniae*, and *S. aureus*).
- All laboratories report using a standardised format.
- All Fleming Fund supported laboratories achieve BSL-2, as per the WHO biosafety manual (e.g. restricted access, biosafety cabinets, relevant SOPs are in place etc).
- Collaboration with the CAPTURA Grant enables provincial supervisory/trouble shooting and generating evidence on AMU and AMC at national and provincial levels.

Output 2.4: Greater clinical engagement

The Fleming Fund aims to develop passive surveillance in the human health sector, where samples and data are collected as part of routine clinical care. The grant therefore emphasises the improvement of clinical engagement at surveillance sites. This will be essential both for ensuring collection of clinical data and increasing the number of tests being performed by laboratories. This will be an important criterion of the success of the grant and will promote sustainability of the surveillance system beyond the Fleming Fund.

The Grantee should focus on building awareness among clinicians at each of the twelve hospitals, positioning the laboratory as a vital aid in helping clinicians make treatment decisions and helping to set and manage reasonable expectations around laboratory functions. At the same time, it will be important to understand the current limitations of the laboratory and to work with laboratory scientists to build confidence in laboratory use.

We invite the grantee to outline strategies to improve clinical engagement and to consider how additional staffing/partnerships could be involved e.g. the involvement of retired professionals and professional groups.

The grantee should also work with clinicians to ensure that key clinical data, e.g. age, syndrome (pneumonia, urinary tract infection, undifferentiated sepsis etc.), severity (e.g. qSOFA score) and whether the infection was community- or hospital-acquired, are included on request forms (either electronic or paper based), so that both laboratory and clinical information are available to inform later analysis.

The grantee should note that the Fleming Fund Country Grant focus is on surveillance, rather than directly supporting the establishment of antimicrobial stewardship programmes (as there are other funding programmes for this). However, the Fleming Fund does aim to ensure the availability and use of data by Antimicrobial Stewardship Committees or Drugs and Therapeutics Committees where these exist. If there is no relevant site committee, the Fleming Fund can support implementation of formal site surveillance groups which involve laboratory staff as well as clinicians, and which are focussed on review of AMR and AMU data (see Annex 5) to inform hospital level prescribing decisions (e.g. developing and auditing treatment guidelines) and to take responsibility for ongoing surveillance activities at the site.

Deliverables:

- Clinicians, laboratory staff and other relevant staff jointly analyse and respond to site-specific AMR and AMU data, either via existing AMS or Drugs and Therapeutics committees, or by establishment of site surveillance committees.
- Laboratory quality management systems include monitoring of reporting turnaround times (for issue of final report and for critical result reporting) to ensure the focus is on providing actionable results for patient care.
- Basic demographic and clinical data are included with sample requests and are available for analysis by the hospital and / or national systems (to include unique patient identifier, date of birth, gender, infection syndrome, community- or hospital-acquired as a minimum).
- Plan developed to establish regular PPSs using the WHO methodology at all FF surveillance sites, to be undertaken by site staff.
- Promotional and communications material for clinical practitioners developed, such as info/training material and bug-drug charts.
- Evidence of successful clinician engagement, as demonstrated by increased sample throughput.

Output 2.5: The private sector shares AMR data

Several large private sector hospitals perform high-volume AST and some also have well-developed networks of sentinel sites across several districts. It is therefore likely that they have a repository of data on AMR. Inclusion of surveillance sites from this sector in the surveillance strategy may be essential for aggregation of more accurate and representative data.

The grantee should work with a small number of private hospitals and the federal or provincial governments to explore how the private sector could be motivated to engage with the national surveillance effort and how private sector data could be shared and contribute to the national picture on AMR and reporting into GLASS.

Under the terms of the Fleming Fund the Grantee cannot provide equipment or reagents for the private sector. However, the Grantee may assist these sites to submit good quality data by including them in training and other capacity building activities provided to government, and by providing appropriate software. The Grantee may also provide support to GoP to assess proposed sites and available data, as appropriate. Consideration should also be given to including them in EQA schemes.

The grantee should note the presence of Regional Grants involved with AMR/AMU retrospective data collection, analysis and dissemination (see section 4) and ensure coordination with any of their efforts directed at the private sector. The management agent can facilitate contact with regional grantees to access information on sites within Pakistan.

Deliverables:

- Select number of private sector labs engaged.
- Tailored training programme on AST delivered.
- Options explored for reporting to the national system, including acceptability and incentives for WHO training and reporting.
- MOUs set up for data sharing between government and private sector at provincial level.
- Private labs (as individual or part of private tertiary care hospitals) participate in EQA systems.

4.3 Objective 3: Sustain existing services and expand AMR surveillance in the animal health sector

Output 3.1: Improved capacity of NVL and NRLPD to function as national reference laboratories for animal health

The National Veterinary Laboratory (NVL) and National Reference Laboratory for Poultry Diseases (NRLPD) are the designated AMR referral laboratories for the animal health sector. Both labs were assessed by the grantee in late 2019. Strengths included the presence of quality assurance managers, mechanisms for sample collection and transportation, and capacity to identify bacterial pathogens and carry out Antimicrobial Susceptibility Testing (AST). Weaknesses included lack of detail in the technical SOPs, limited capacity for genomic sequencing, significant gaps in biosafety and an absence of biorepository arrangements. Neither of the laboratories were enrolled in an EQAS service for AMR testing, nor did either of them have standards for reporting results. NRLPD had very limited space for bacteriology work.

On the basis of this assessment the grantee formulated, and has started to implement, capacity development plans, including comprehensive refurbishment, procurement of equipment, reagents and consumables, and training, in line with the requirements of ISO 17025.

Under CG2 the grantee should ensure that NVL and NRLPD have the capacity to achieve and maintain the specified 'core' functions by the end of the grant (see Annex 1). Progress will be monitored on a quarterly basis. Other extended or advanced functions can be considered for Pakistan if the grantee is able to provide sufficient justification.

Our expectation is that by the end of the grant, in addition to the core functions, NVL and NRLPD will be able to perform:

- confirmatory testing – ID, resistance mechanism determination (e.g. identify ESBL producers, CREs, MRSA), MIC testing.
- QC – checking 10% of isolates from sentinel sites for correct ID and AST results with supportive corrective measures if performing poorly.

Priority pathogens for CG2 are *E. coli*, *Enterococcus* spp., *Salmonella* and *Campylobacter* spp. in line with the priorities of the national surveillance strategy.

The grantee has started to address gaps in the biorepositories at NVL and NRLPD. The required standard for implementation under CG2, if not already achieved, is a secure -80°C freezer, a database, and SOPs for storage, access and use, and sharing of isolates. If the repository is a single freezer, a Microsoft Excel spreadsheet to log isolate position and number will be adequate.

Some progress has already been towards improving biosafety at both sites. Under CG2 the grantee will be required to prioritise attainment and retention of biosafety level 2 (BSL-2) for both laboratories, if this has not already been achieved under CG1. This should be verified by independent assessment with the cost of the assessment included in the Country Grant.

Both laboratories have LIMS, but neither are functional. Meanwhile paper systems are being used. The grantee should work with NVL and NRLPD to enable them to maintain an up-to-date and accurate database of demographic details together with matched culture, identification and AST results for each sample they process, using WHONET. Data should then be regularly sent for analysis,

ideally to MoNFSR's AHC office (see Objective 1, Output 1.1). The grantee should ensure that data can be exported in a WHONET-compatible format to facilitate national collation and reporting.

The grantee should also include within their budget the cost of laboratory assessments at the end of the grant, to measure progress from the initial assessments.

Deliverables:

- NVL and NRLPD achieve and maintain the specified 'core' functions by the end of the grant (see Annex 1).
- NVL and NRLPD perform confirmatory testing – ID, resistance mechanism determination (e.g. identify ESBL producers, CREs, MRSA), MIC testing.
- NVL and NRLPD perform QC – checking 10% of isolates from sentinel sites for correct ID and AST results with corrective measures if performing poorly.
- NVL and NRLPD can perform bacterial ID and AST for *E. coli*, *Enterococcus* spp., *Salmonella* and *Campylobacter* spp. at an acceptable standard.
- NVL and NRLPD are enrolled and participate in an international EQA scheme.
- Progress is made towards ISO 17025 accreditation.
- A biorisk management system is established, with emphasis on development of institutional biosafety manuals, capacity development of laboratory staff and rectifying other areas of concern identified in assessments.
- NVL and NRLPD achieve and retain biosafety level 2 (BSL-2).
- LIMS at NVL and NRLPD are activated and inter-operable with WHONET.
- A biorepository is in place

Output 3.2: Implementation of active surveillance progressed

A National Surveillance Strategy for Antimicrobial Resistance in Healthy Food Animals has been formulated under CG1. This focuses on commensal bacteria (*E. coli*, *Enterococcus* spp.) and zoonotic foodborne bacteria (*Salmonella* and *Campylobacter* spp.) in poultry and large ruminants (cattle and buffalo).

In addition, and in line with the national surveillance strategy, the grantee is supporting the implementation of a pilot surveillance programme for AMR in clinically healthy animals from selected production systems i.e. commercial broilers and bovines intended for slaughter. The pilot will focus on commensal bacteria (*E. coli*, *Enterococcus* spp.) and will focus on five districts, one in each of Islamabad Capital Territory, Punjab, Sindh, Baluchistan and KP. COVID-19 permitting, the pilot is expected to be completed and results analysed by the end of the grant. Samples will be analysed by NVL and NRLPD.

Under CG2 the grantee should support further implementation of active surveillance, in line with the national surveillance strategy and the findings of the pilot study. The surveillance pilot should be expanded to include more sites, and/or small ruminants, and/or more production systems, according to time available.

The pilot should also include the nine animal health laboratories identified for capacity building (see output 3.3) as a way of facilitating passive surveillance (see output 3.4).

The grantee should facilitate the involvement of provincial governments in the active surveillance effort, engaging them as much as possible in coordination and implementation of the surveillance

itself (as stated in the surveillance strategy) and enabling them to start to use the results of the data analysis.

In line with the national surveillance strategy both laboratory findings and field data should be shared with the Federal Epidemiology Unit (FEU) under the AHC office. This will need to be reactivated to carry out data management, analysis and dissemination to relevant stakeholders, including public health counterparts, to foster a ‘One Health’ approach for AMR surveillance in Pakistan. The grantee should provide capacity building support to the FEU to enable it to carry out this function.

The cost of reagents and consumables for active surveillance should be included within the cost of the grant. Those items should be procured by the grantee.

Expansion of active surveillance to aquaculture could be considered but will be dependent on the capacity of the relevant laboratory. The grantee should carry out a laboratory assessment and present a costed plan for discussion with the management agent for consideration if the budget allows. Meanwhile staff from the laboratory could be included in existing training.

Deliverables:

- Active AMR surveillance strategy and pilot expanded to include (according to time available) more sites, and/or small ruminants and/or more production systems.
- All nine peripheral laboratories participate in active surveillance (according to their capacity).
- Federal Epidemiology Unit for AH carries out data management, analysis and dissemination to relevant stakeholders.
- Needs assessment carried out at the aquatic laboratory.
- Costed plan for aquatic laboratory strengthening developed, for consideration by the MA.

Output 3.3: Nine provincial peripheral laboratories participate effectively in the national surveillance effort.

The National Surveillance Strategy for Antimicrobial Resistance in Healthy Food Animals proposes that provincial peripheral laboratories should eventually be able to carry out processing and diagnostics for samples collected for national active surveillance, as resources become available and their capacity is enhanced.

Nine laboratories were assessed by the grantee in October/November 2019. The assessments indicated that the labs currently have some capacity, but many aspects require strengthening – see Table 4.

Table 4: Overview of Animal Health Laboratories by Region¹⁰

| Region | Laboratory | Capacity | | | |
|------------------|----------------|----------------|-------|------------|-----|
| | | Infrastructure | Media | ID and AST | QMS |
| Gilgit-Baltistan | DDL, Gilgit | | | | |
| Sindh | PRI, Karachi | | | | |
| | CVDL Tando Jam | | | | |

¹⁰ AMR Sentinel Sites Readiness Assessment, R. Dacombe, January 2020, p.23

| Region | Laboratory | Capacity | | | |
|--------------------|-------------------|----------------|--------|------------|--------|
| | | Infrastructure | Media | ID and AST | QMS |
| Punjab | PDDL, Lahore | Orange | Orange | Red | Red |
| | PRI, Rawalpindi | Orange | Orange | Orange | Orange |
| Khyber Pakhtunkhwa | DIL, Peshawar | Orange | Orange | Red | Red |
| | PRI, Mansehra | Orange | Orange | Red | Red |
| Kashmir | DDL, Muzaffarabad | Red | Orange | Red | Red |
| Baluchistan | DIL, Quetta | Red | Orange | Red | Red |

Key: **Green** - no support required; **orange** - some capacity which requires strengthening; **red** – no or extremely limited capacity.

Infrastructure was found to be acceptable, with most sites having back-up power and access to distilled water, but most of the laboratories had limited equipment or capacity to support bacteriology, including bacterial identification and AST. Safety was an issue in most places due to a lack of both equipment and processes. In addition, all of them were using paper-based recording systems.

The grantee has proposed an initial capacity building plan for all the laboratories, including training in basic bacteriology methods, and an introduction to WHONET use and data reporting. No procurement is planned for these laboratories under CG1.

CG2 will support all the laboratories listed above in a phased approach, taking account of the variable capacities and the extent of refurbishment and equipment provision required. Capacity development should be:

- In line with decisions on how active surveillance is to be rolled out (as stated in the National Surveillance Strategy and informed by the results of the six-month surveillance pilot study).
- Carried out in consultation with the relevant provincial governments, taking into account their willingness and capacity to engage with, support and benefit from provincial level AMR data.
- Based on agreement on how peripheral provincial laboratories can become integral to the national surveillance system.

By the end of CG2 the selected laboratories should have the capacity to process faecal, cloacal and caecal samples, and perform bacterial culture, ID and AST for *E. coli* and *Salmonella*. More widely, the grantee should ensure that the laboratories have the capacity to achieve the specified 'core' functionalities by the end of the grant (see Annex 1), prioritising activities that will help to achieve that goal. Progress will be monitored on a quarterly basis. Progress beyond 'core' is not required for peripheral laboratories.

The grantee will be required to prioritise attainment and retention of biosafety level 2 (BSL-2) for the provincial peripheral laboratories. This should be verified by independent assessment, with the cost of the assessment included in the Country Grant.

The grantee will also need to support implementation of WHONET at the surveillance sites, or if a functioning LIMS is in place, should ensure that data can be exported to WHONET, if required.

The grantee should also include within their budget the cost of the 9 laboratory assessments at the end of the grant, to measure progress from the initial assessments.

Deliverables:

- All laboratories have made clear progress towards sustainable capacity to process faecal, cloacal and caecal samples, and perform bacterial culture, ID and AST for *E. coli* and *Salmonella*.
- All laboratories have made clear progress towards achieving the specified 'core' functions by the end of the grant (see Annex 1).
- All laboratories have in place basic requirements for BSL 2 as per the OIE terrestrial manual (Chapter 1.1.4 on biosafety and biosecurity - restricted access, biosafety cabinets etc.) and relevant SOPs are in place.
- All laboratories are enrolled in national EQA programmes delivered by the NRLs

Output 3.4: Passive surveillance initiated

In addition to engaging the peripheral provincial laboratories in active surveillance, the grantee should also encourage the implementation of passive surveillance in those nine laboratories where capacity is being built, and the two reference laboratories. The grantee will be expected to develop strategies to work with the relevant provincial governments to implement passive surveillance and to use the results. This should include a plan for a gradual shift from active (see output 3.2) to a mixture of active and passive surveillance.

The grantee will need to develop strategies to encourage animal health professionals and livestock keepers to make greater use of laboratory services as informed by the KAP survey carried out under output 1.4. and the AH PPS carried out under CG1. This might include:

- Developing programmes to drive demand for improved diagnostics and data.
- Developing strategies to increase demand for microbiology testing as a way of promoting use and sustainability of laboratories.
- Strengthen the best performing laboratories' capacity to culture, identify and carry out ASTs on the three most frequent bacterial pathogens of interest to veterinary medicine that can be safely cultured given the current biosafety and biosecurity levels.
- Providing support to amend the training curriculum of animal health prescribers.

The grantee must include in their budget sufficient funds for reagents and consumables for any additional costs of passive surveillance (i.e. collection, transport and processing of clinical samples) undertaken within this grant. These should be on top of the costs normally covered by government and the grantee should ensure that funds are not displacing normal government spending. In the interests of capacity building and sustainability, the grantee should support government, either at the federal or provincial levels, to carry out the procurement and should then reimburse for the cost of the items.

Deliverables:

- National surveillance strategy developed for sick animals.
- Communication packages developed for farmers, veterinarians and paravets regarding use of laboratory services and antimicrobials in animals.
- Recommendations developed for amendment of training curricula of veterinarians and pharmacists on the use of antimicrobials and the importance of diagnostic testing for AMR.

- Provincial governments are engaged in the development of passive surveillance and use of results.
- Supported laboratories initiate passive surveillance in sick animals.

5 Grantee Roles and Responsibilities

The main role of the Grantee – or Lead Grantee if the successful applicant is a consortium – will be to plan and implement the outputs and deliver the objectives listed above. The Grantee will be responsible for providing the expert technical assistance and high-quality support needed to achieve agreed results. The Lead Grantee will also be responsible for financial management and controls for the entire grant, including the contributions of sub-grantees if applicable, and for monitoring and 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.

6 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 the suggested indicators may not all be applicable. Therefore, applicants are expected to select from the standard indicator set only where appropriate.

In summary, while the completion and level of attainment for all activities require 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 or are too advanced).

In addition to measuring grant performance against the objectives and outputs stated above, the grant will also be monitored for the implementation of, and adherence to, the Fleming Fund core principles described in Section 2.4, and the practical implications of this will be discussed with the successful applicant.

7 Application requirements

7.1 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 laboratory capacity development, surveillance, capacity building and OH.
- Must have experience of programme implementation in Pakistan.

- Must demonstrate that they are registered to work within the country, including the provision of essential documents, such as articles of incorporation.
- 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 consortium.
- 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 consortium, 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 institute;
 - Non-governmental organisations (NGOs);
 - UN Agencies;
 - Private companies; or
 - 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.
- In line with UK Government financial transparency requirements any for-profit organisations will be asked to declare profit levels.

7.2 How to apply

Prospective Grantee must write to flemingfundSEA@mottmac.com to confirm the name, phone number and email address of their main focal point. An official Application Pack will be sent out to the nominated focal point on the date mentioned below in Section 7.5. To apply, please complete the application form and the budget and monitoring template, 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 TOR.
- When submitting the application document, press “Reply All” from the Application Pack email that you received 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 in 2 (above) using “Reply All”.
- 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 are likely not to be accepted.

7.3 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).

We emphasise that the ultimate purpose of these investments is to further strengthen and transform Pakistan’s approach to AMR prevention and control in line with the country’s Strategic Plan. We will therefore be giving preference to those applications that have:

- A clear, well-articulated, practical and feasible approach to addressing the most important strategic bottlenecks and gaps in Pakistan’s existing system.
- Key team members proposed by the Grantee and partners, with required management and/or technical experience and skills to deliver the project activities.
- Clearly laid out project management plan, consortium management plan (if proposed) and operational plan.
- Ability and preparedness to bring stakeholders together in an effective and productive working arrangement, promoting a OH approach.
- Demonstrated value for money, including concepts such as total overall costs over the life of an activity and not simply lowest cost.
- Demonstrated ability to work effectively across multiple sectors.
- Documented evidence of the ability to operate in Pakistan.

7.4 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.

7.5 Key dates

- TOR shared with selected candidate: **24 August 2020.**
- Application submission deadline: **25 September 2020 17.00 PKT (GMT+5)**
- Anticipated start of grant: **1 November 2020**

7.6 Contact details and support information

Any questions on the Terms of Reference should be sent to flemingfundSEA@mottmac.com. Mott MacDonald will endeavour to respond to queries within three working days.

8 Fleming Fund 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.