

Terms of Reference for Request for Proposals

First Fleming Fund Country Grant to Bhutan

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 Bhutan. It has been created in response to a Request for Support from the Royal Government of Bhutan (RGOB). The grant will be funded by the UK Department of Health and Social Care (DHSC), under its Fleming Fund Grants Programme, which is managed by Mott MacDonald, the Management Agent.

This first Fleming Fund Country Grant for Bhutan 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.

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, if any, on the same back-to-back terms.

This grant is expected to last 18 months while subsequent grants may be made available for later years. The value of the first Country Grant for Bhutan is expected to be up to £1.5million, including 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.¹

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

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

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, 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 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 Susceptibility Testing.
- 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. Grantee is expected to adhere to and demonstrate this alignment and contribution to outputs in the application. A description of each output is provided in this RFP for the applicant to develop specific, measurable and budgeted activities that are well organised and phased to ensure the success of the implementation of the Country Grant.

2.4 Core principles within the Fleming Fund Grants Programme

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

- 1) Country Ownership:** The Fleming Fund Grants Programme will be implemented in line with national plans and aspirations, as laid out in the National Action Plan. 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 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 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 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 be for duration of approximately 18 months, providing structured learning, mentoring and skills development for four to eight Fellows in each project 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

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.

Institution 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.

Mott MacDonald will be developing detailed Terms of References (TORs) for the Fellowships for Bhutan, and the Fellowships finalisation process is expected 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 Bhutan to date

This is the first Fleming Fund Country Grant to be released in Bhutan. In preparation for this grant Mott MacDonald, carried out a Scoping Visit in January 2018 which was followed by Positioning Activities in March 2018 to refine the design of surveillance systems and conduct laboratory assessments, in order to better understand the priority areas to be supported through this RFP.

These activities culminated in identification of the major gaps and needs for strengthening AMR and AMU surveillance in humans and animals, and informed agreement with the Royal Government of Bhutan about grant objectives and outputs.

3 The current AMR situation in Bhutan

3.1 National AMR landscape

Bhutan has developed National Action Plan (NAP) on Antimicrobial Resistance (2017 – 2020) which has been endorsed by Cabinet and approved by the Ministry of Health. 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 not all have funding. The Drug Technical Advisory Committee (DTAC) with expanded members from Bhutan Agriculture and Food Regulatory Authority (BAFRA), Royal Centre for Disease Control (RCDC) was identified as the National AMR Technical Committee for AMR. It consists of 9 DTAC members plus one each member from BAFRA and RCDC. The highest policy decision making bodies for AMR is the Inter-Ministerial Committee for One Health (IMCOH) approved under the Bhutan One Health Strategic Plan by the Cabinet, and this system integrate AMR management in Bhutan under One Health approach.

3.2 One Health

The Royal Government of Bhutan has approved Bhutan One Health Strategic Plan (2017 – 2022) that would strengthen and encourage multi-sectoral One Health approach towards prevention and control of zoonotic diseases, other emerging infectious diseases, high-impact non-communicable disease including containment of AMR problems. There is a Memorandum of Understanding (MoU) amongst the Ministry of Health and Ministry of Agriculture and Forestry, Khesar Gyalpo University of Medical Sciences of Bhutan, Royal University of Bhutan, Ministry of Home and Cultural Affairs which guides the collaboration and implementation of activities related to One Health. One of the key activities identified in the strategic plan is AMR. The Royal Government of Bhutan 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

Bhutan is in the early stages of defining its approach to AMR surveillance. Laboratory capacity for pathogen identification and Antimicrobial Susceptibility Testing is available at Jigme Dorji Wangchuck National Referral Hospital (JDWRH) and the Royal Center for Disease Control for enteric pathogens (previously the National Public Health Laboratory) located in Thimphu. Additional AMR capacity exists at 2 regional level hospital

laboratories - Gelephu, and Mongar; and 1 district level hospital at Phuentsholing. There are no microbiology laboratories at other district hospitals. In addition, an AMR stewardship unit, coordinated by a clinical pharmacologist is established at JDWNRH.

3.4 AMR Surveillance – animal health

While there is no formal AMR surveillance in livestock, the NCAH (National Referral Veterinary Laboratory) conducts antibiotic susceptibility testing (AST) on some samples from clinically ill or dead animals. The laboratory has previously conducted a project on ESBL+ *E coli* in pigs with the support of the Institute of Food Science and Hygiene, University of Zurich, Switzerland. Some studies have been conducted on AMR in *Salmonella* in locally produced and imported chicken meat. Bhutan has been provided with US\$15000 for a WHO Advisory Group on Integrated Surveillance of Antimicrobial (AGISAR) project to test for resistance in *Salmonella* spp in humans, livestock and food. No support other than financial is provided through this project. The regional veterinary laboratories (4 located at Chukha, Wangdiphodrang, Zhemgang and Trashigang) have the capacity to carry out culture and isolation of bacteria and conduct AST on some samples from clinically ill or dead animals. However, there is a need to strengthen the AST skills and processes in regional laboratories to produce reliable results.

4 Scope of this Country Grant

4.1 Grant Objectives and Outputs

Grant objectives and outputs are summarised as follows. A detailed description of each output is provided in Annex 1. 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).

Objective 1: Establish a One Health governance structure that spearheads the activities of AMR and AMU surveillance

- Output 1.1: Inter-Ministerial Committee for One Health (IMCOH) is functioning as the policy-level decision making body for addressing AMR in Bhutan.
- Output 1.2: The One Health Secretariat provides support for the National AMR Technical Committee according to a NATC-agreed TOR.
- Output 1.3: A National AMR Technical Committee (NATC) is established with an agreed ToR and quarterly meetings held.
- Output 1.4: Quarterly and annual reports showing a comparison of the AMR and AMU patterns in humans and animals are sent to the surveillance stakeholders.
- Output 1.5: Evidence-based recommendations for further AMR/AMU surveillance and for AMU-related policies are provided to the IMCOH.
- Output 1.6: A national symposium on AMR and AMU is delivered towards the end of the grant period.

Objective 2: Strengthen AMR and AMU surveillance in humans

- Output 2.1: A MOH AMR/AMU Surveillance TWG functioning in accordance with a NATC-approved TOR.
- Output 2.2: JDWNRH is functioning as the clinical reference centre supporting the AMR surveillance system with a NATC-approved TOR.
- Output 2.3: The Royal Centre for Disease Control (RCDC) is functioning as a reference centre for AMR in enteric pathogens and organise a bio repository with a NATC-approved TOR.
- Output 2.4: The bacteriology laboratories at Gelephu Regional Referral Hospital, Mongar Regional Referral Hospital and Phuentsholing General Hospital generate quality assured AMR data.

- Output 2.5: Biosafety and biosecurity measures are in place at reference centers, surveillance sites and for the transportation of samples and strains within the network.
- Output 2.6: Surveillance sites are regularly sending quality AMR, clinical and basic epidemiological data to JDWNRH.
- Output 2.7: Quarterly and annual reports of AMR established surveillance results produced by RCDC are shared with the MoH AMR and AMU TWG, the NATC and the surveillance sites.
- Output 2.8: Capacity and needs assessment completed for 3 additional surveillance sites using the Fleming Fund Human Health surveillance site assessment tool.
- Output 2.9: At least 3 biomedical engineers from the Department of Medical Supplies & Health Services/MOH are trained and accredited.

Objective 3: Strengthen AMR and AMU surveillance in food animals

- Output 3.1: A MOAF AMR and AMU Surveillance TWG is functioning in accordance with a NATC-approved TOR.
- Output 3.2: National Veterinary Laboratory (NVL) is functioning as the AMR reference laboratory.
- Output 3.3: NVL, and Chukha & Trashigang Regional Livestock Development Centre (RLDCs), & NFTL produce reliable quality bacterial culture, identification and Antibiotic Susceptibility Test (AST) results for *E. coli*, *Klebsiella*, *Salmonella* and *Enterococci*.
- Output 3.4: NVL and NFTL have the capacity to culture *Campylobacter*.
- Output 3.5: Biosafety and biosecurity measures are being applied within NVL, the two regional laboratories and the NFTL and to the safe transport of samples and isolates between the laboratories.
- Output 3.6: Good quality samples from healthy layer hens and broilers are regularly sent to NVL, CRLDC and TRLDC for culture and AST, according to the agreed schedule.
- Output 3.7: Good quality samples from locally grown chicken meat are regularly sent from meat shops in Thimphu to NFTL for culture and AST, according to the agreed schedule.
- Output 3.8: A national database of verified AMR results and associated demographic data is maintained in WHONET at the NVL.
- Output 3.9: National Centre for Animal Health (NCAH) shares quarterly and annual reports of AMR and AMU surveillance results with the MOAF AMR and AMU Surveillance TWG, the NATC and the RLDCs.
- Output 3.10: Extended G2C database for electronically recording prescription and antibiotic use data in veterinary districts is recommended.

4.2 Duration of the grant

The grant is expected to be implemented for 18 months. A second, subsequent Country Grant may be available to Bhutan, dependent upon successful implementation of the first Country Grant.

4.3 Funding envelope

Grant applications are expected up to £1.5 million, including 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 could be considered as part of a Value for Money (VfM) approach and an indication of how we may assess VfM.

4.4 Procurement

Lab equipment and consumables

An indicative procurement list for lab equipment and consumables for Bhutan was compiled following site assessments that were undertaken during the Positioning Activities. The procurement list will be included as

part of the Application Pack for information purposes only. The applicant should not budget for the procurement of lab equipment and consumables.

In the first month of the Country Grant, the grantee will need to finalise the detailed specifications of equipment and consumables. A decision will be made by the Management Agent, in consultation with the grantee, the Management Agent's procurement supplier (International Procurement Agency) and DHSC, with regard the most suitable method of procurement for lab equipment and consumables. Even if equipment and consumables are not procured by the Grantee, it will still have five key roles with regard the items:

1. to assist with the importation and delivery of equipment and consumables to recipient sites;
2. to work closely with the organisation that does the procurement to ensure delivery of items are sequenced appropriately;
3. to maintain an asset register of all items that are defined as assets by the programme;
4. to regularly monitor the items that have been procured by Fleming Fund Grants Programme throughout the course of the grant to ensure: i) items are being used for intended use; and ii) items are being maintained appropriately; and
5. to report any misuse or misappropriation of assets to the Management Agent.

Renovation of labs

Three labs (Gelephu Regional Referral Hospital, Mongar Regional Referral Hospital and Phuentsoling General Hospital) have been identified for renovation in the first Fleming Fund Country Grant. Grantee will be required to carry out the renovation of the three labs. The Grantee will be responsible for procuring any other goods (for example 'laboratory infrastructure' in the procurement list) that are required for the renovation of labs (e.g. bench tops, AC units, flooring, generator etc). The Grantee should provide an estimated budget for these costs under a dedicated activity in its proposal. For all items procured under renovations, the Grantee will be responsible for:

1. to maintain an asset register of all items that are defined as assets by the programme;
2. to regularly monitor the items that have been procured by Fleming Fund Grants Programme throughout the course of the grant to ensure: i) items are being used for intended use; and ii) items are being maintained appropriately; and
3. to report any misuse or misappropriation of assets to the Management Agent.

5 Grantee Roles and Responsibilities

The main role of the Grantee will be to plan and execute outputs and deliver the objectives listed above. The Grant is designed as an AMR laboratory capacity building and systems strengthening intervention. The 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 strengthen the selected reference and surveillance sites' capability and capacity to generate and share AMR surveillance data on both a national and international basis.

6 Key measures of success

Country Grants will eventually be 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, for the first Country Grant, it is important to note that:

- (i) Applicants are not expected to select from and use these indicators for this first Country Grant. While it is possible that some of the formal indicators may trigger towards later stages of

the grant award, the likelihood of this will be reviewed and discussed by Mott MacDonald with the successful applicant.

- (ii) For the purposes of this first grant, process level indicators will be used to track progress against the work plan. The Grantee is expected to utilise the indicators proposed above or to propose alternative SMART indicators in line with the outputs summarised above.⁴ These will then be negotiated and agreed with Mott MacDonald as the Management Agent.
- (iii) No Country Grant will be expected to use all the Fleming Fund indicators. Instead a relevant *subset* of indicators will be proposed by the Grantee for joint agreement with Mott MacDonald.
- (iv) The Fleming Fund will be independently evaluated by Itad, a specialist evaluation firm, who have been appointed by the UK Department of Health and Social Care for this purpose. 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 grant principles described above. All grants are subject to review and evaluation by the evaluators, and full co-operation with the evaluators by all Grantees is expected.

7 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, future absorptive capacity, alignment with others AMR related initiatives such as those undertaken by multilateral agencies such as WHO and FAO. In addition, the Grantee will need to build strong collaboration and coordination with local academic and research institutions at different levels for technical and other support.

8 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 and Regional Grants.

According to current plans, six Fleming Fellowships, from both the human health and animal health sectors, will be issued in Bhutan (see Annex 2). Successful applicants will receive specialised training in AMR and AMU data management and analysis, laboratory quality management, and in advanced laboratory technical skills.

Fellows are expected to become technical leaders in AMR and AMU surveillance in Bhutan, 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). Annex 2 outlines the likely location and scope of the Fellowships.

Additionally, 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.

⁴ SMART indicators refers to indicators that are specific, measurable, achievable, relevant, and time bound.

9 Application requirements

9.1 Grant Eligibility Criteria

This is a single source RFP. An application is invited only from one of the ministries or departments of the RGOB. Please note that we are seeking only one single application. In case more than one ministry or department is applying in response to this RFP, then they should apply in a partnership, with one ministry or department proposed as Lead Grantee.

9.2 How to apply

An email expressing interest should be sent to flemingfundSA@mottmac.com by **6 June 2018** in order to receive **the Application Pack**.

The Applicant Information Session (AIS) will be organised in Thimphu on 3rd and 4th July 2018, to provide detailed orientation on the application completion process, and to clarify doubts with regard to the RFP or the application process.

Ahead of the AIS, the Application Pack will be shared and will include the application form, budget and monitoring template, and Guidance Notes.

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

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

- The application submission should be returned by the deadline indicated in the RFP.
- 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 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 and will be returned.

9.3 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 will be assessing the application on following key areas:

- 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

9.4 Restrictions/limitations

Only RGoB is invited to respond to this RFP.

Some restrictions may apply to what could be budgeted under the Country Grant. The applicant is advised to refer to the Application Pack for further information.

9.5 Key dates

Publication of RFP: 31 May 2018

Deadline for registering interest to receive the Application Pack: 6 June 2018

Applicant Information Session: 3 and 4 July 2018

Application deadline: 12 July 2018, 1700 Hrs BST

Anticipated start date of grant: 1 October 2018

9.6 Contact details and support information

Any questions on the Request for Proposals should be sent to flemingfundSA@mottmac.com. Mott MacDonald will endeavour to respond to queries within three working days.

10 Annex 1: Detailed Objectives and Outputs

10.1 Objective 1: Establish a One Health governance structure that spearheads the activities of AMR and AMU surveillance

Output 1.1: Inter-Ministerial Committee for One Health (IMCOH) is functioning as the policy-level decision making body for addressing AMR in Bhutan

The Inter-Ministerial Committee for One Health (IMCOH) was approved under the Bhutan One Health Strategic Plan by the Cabinet on 22 November 2016 vide approval letter no. C-3/119/539 dated 22 December 2018. IMCOH has Secretaries of MOH and MOAF, Heads of Department of Public Health, Department of Medical Services, Royal Centre for Disease Control, Department of Livestock, Bhutan Agriculture and Food Regulatory Authority (BAFRA), Department of Forests and Park Services, Department of Disaster Management, Faculty of Nursing and Public Health of Khesar Gyalpo University of Medical Sciences of Bhutan, and College of Natural Resources of Royal University of Bhutan. The IMCOH is chaired by the Secretaries of MOH and MOAF on a rotational basis. The Secretary, MOH is the current Chair of IMCOH.

This existing inter-ministerial structure would be the most appropriate multi-sectoral governance body to make high-level decisions on priority areas for investment in AMR and AMU surveillance and for programmes and/or policies to improve antibiotic use in Bhutan. The IMCOH would be supported by the National AMR Technical Committee (NATC) who would make recommendations to the IMCOH for high-level decisions.

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

- IMCOH will have met at least once, and made decisions based on the recommendations from the NATC on future surveillance priorities and/or programmes or policies to improve responsible antibiotic use in Bhutan.
- Active participation of human and animal health sectors in the meeting(s).

Output 1.2: One Health Secretariat provides secretariat support for the National AMR Technical Committee according to a NATC-agreed ToR.

Establishment of a One Health Secretariat was approved under the Bhutan One Health Strategic Plan by the Cabinet vide approval letter no. C-3/119/539 dated 22 December 2018. To date, there has been no funding available to establish this One Health Secretariat. The Fleming Fund provides an opportunity to establish the One Health Secretariat with a role in providing secretariat support to the multi-sectoral NATC.

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

- The One Health Secretariat office is established with one staff member each from MoH and MoAF supported by one administrative-Finance staff, office furniture and a computer– information regarding the physical localisation of the secretariat will be provided by the NATC
- The Secretariat is operating with a ToR agreed by the NATC.
- The Secretariat has organised quarterly meetings for the NATC.
- The Secretariat maintains a written record of NATC meetings, including participants, an agenda and key decisions from the meeting.
- The Secretariat maintains a national repository of reports and any other technical documents from the sector-based surveillance TWGs that are discussed during NATC meetings.

Output 1.3: A National AMR Technical Committee (NATC) is established with an agreed ToR and quarterly meetings held.

The current Drug Technical Advisory Committee (DTAC) has been functioning as the lead technical committee for AMR to date. It is recognised that the DTAC membership needs to be expanded to form a broader National

AMR Technical Committee which will address AMR and AMU surveillance. The expanded committee will include representatives from BAFRA, RCDC and Department of Agriculture. This committee will be the leading national technical committee that:

- Reviews the information on AMR and AMU in humans and animals that has been generated through the Fleming Fund Country Grant and the Fleming Fellowship Scheme (FFS).
- Combines this with other information on AMR and AMU generated through other programmes in Bhutan.
- Interprets the AMR findings in humans and animals in the context of the AMU information from humans and animals.
- Summarises the current state of knowledge on AMR and AMU in Bhutan.
- Prepares a set of recommendations regarding priorities for future surveillance.
- Presents results in a way that is accessible to policy makers and including recommendations for policy and practice that would improve the appropriate use of antibiotics
- Identifies opportunities for collaboration between human animal and other sectors wherever possible, e.g. in training programmes, quality assurance systems, procurement and logistics, etc.

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

- The NATC is functioning in accordance with a ToR
- NATC has met at least every quarter to review progress with AMR and AMU surveillance.
- Improved multi-sectoral understanding of AMR and AMU in Bhutan.

Output 1.4: Quarterly and annual reports showing a comparison of the AMR and AMU patterns in humans and animals are sent to the surveillance stakeholders.

The NATC is responsible for producing a collated report that brings together all the information collected through AMR and AMU surveillance, including:

- A description of surveillance methodologies
- Results to date
- Interpretation and discussion of the results
- Recommendations for enhancements to existing surveillance, new surveillance, and/or investigations

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

- NATC has produced quarterly and annual reports.
- Reports from each of the TWGs and a multi-sectoral report combining all results is produced following each meeting.

Output 1.5: Evidence-based recommendations for further AMR/AMU surveillance and for AMU-related policies are provided to the IMCOH.

Towards the end of the grant period NATC will be in a position to review all the information obtained through the AMR and AMU surveillance programmes, and to summarise what the surveillance has contributed to knowledge of AMR patterns and drivers in Bhutan.

Based on these findings NATC will prepare a set of recommendations for the IMCOH on:

- Future AMR and AMU surveillance and investigation priorities
- Programmes, approaches or policies to improve responsible use of antibiotics in humans and/or animals.

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

- NATC has provided at least one set of recommendations to IMCOH on future AMR/AMU surveillance priorities and on programmes or policies to improve responsible use of antibiotics in humans and/or animals.

Output 1.6: A national symposium on AMR and AMU delivered towards the end of the grant period.

Organising a national symposium on AMR and AMU in Bhutan towards the end of the grant period provides an excellent focus to bring together and evaluate all the information that has been generated through the grant period and identify the contribution of this to understanding AMR and AMU in Bhutan. This provides the opportunity to present the results of the work conducted during the grant period, and to identify the current state of knowledge on AMR and AMU.

It will be the responsibility of the NATC and its secretariat to organise a national AMR symposium for Bhutan. 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.

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

- A national AMR symposium is successfully delivered.
- Active participation in the symposium by the human and animal health sectors and wider AMR stakeholders.
- Improved cross-sectoral understanding of AMR and AMU in Bhutan.

10.2 Objective 2: Strengthen AMR and AMU surveillance in humans

AMR and AMU surveillance in the human sector will focus on strengthening reference centers and regional hospitals under the overall guidance of a MoH-led AMR and AMU Surveillance Technical Working Group. The NTAC has selected Jigme Dorji Wangchuck National Referral Hospital (JDWNRH) and the Royal Centre for Disease Control (RCDC) to assist the surveillance sites in the collection of quality assured AMR and AMU data following international Biosafety and Biosecurity standards.

A list of priority specimens and priority pathogens following WHO's GLASS recommendations and incorporating national priorities has been developed (see table 2 below). The resistance patterns to antibiotics and the mechanism of resistance for these priority pathogens will be obtained in priority from blood, urine and stool samples at all sites and from urethral and cervical swabs from Regional Referral hospital laboratories.

The 3 proposed human health fellows (laboratory, AMR and AMU surveillance, see annex 2) would provide leadership and technical support for the TWG and reference centres.

Table 1: List of reference centers and surveillance sites to be strengthened through the first Fleming Fund Country Grant

Category	Name	Location
Clinical Reference Lab	Jigme Dorji Wangchuck National Referral Hospital (JDWNRH)	Thimphu
Epidemiology Reference Lab	Royal Centre for Disease Control (RCDC)	Thimphu
Surveillance site	Gelephu Regional Referral Hospital	Gelephu
Surveillance site	Regional Referral Hospital	Mongar
Surveillance site	Phuentsoling General Hospital	Phuentsoling

Table 2: Priority pathogens to consider for surveillance

	Pathogens	Collection sites	Primary Referral Centre
GLASS priority pathogens	<i>Escherichia coli</i>	All sites	JDWNRH
	<i>Escherichia coli (stool)</i>	All sites	RCDC
	<i>Klebsiella pneumoniae</i>	All sites	JDWNRH
	<i>Acinetobacter baumannii</i>	All sites	JDWNRH
	<i>Salmonella spp</i>	All sites	RCDC
	<i>Shigella spp.</i>	All sites	RCDC
	<i>Staphylococcus aureus</i>	All sites	JDWNRH
	<i>Streptococcus pneumoniae</i>	All sites	JDWNRH
	<i>Neisseria gonorrhoeae</i>	Regional labs	JDWNRH
National priority pathogen	<i>Clostridium difficile</i>	JDWNRH	JDWNRH
	<i>Pseudomonas aeruginosa</i>	JDWNRH	JDWNRH

Output 2.1: A MOH AMR and AMU Surveillance TWG functioning in accordance with a NATC-approved ToR

The TWG should include relevant technical experts and stakeholders in AMR and AMU surveillance in the human health sector. A typical committee may include: clinical microbiologists, epidemiologists, pharmacist, data manager, laboratory manager, hospital managers etc. from a variety of institutions or departments within MOH. Suggested roles and responsibilities to be validated by NATC in a ToR are described below:

- Define objectives and provide technical guidance for stepwise implementation of a sustainable AMR surveillance system in the Human health sector based on the selection of national priority specimens and pathogens.
- Organise and lead the revision of standards (CLSI or EUCAST), protocols and guidelines to harmonise AMR testing across the surveillance sites (Quality Assurance Manual; Laboratory Diagnostic SOPs and flowcharts on pathogen identification and Antibiotic Susceptibility Testing, etc.) and coordinate their dissemination in collaboration with the reference centres.
- Provide guidance and information on clinical, epidemiological and laboratory data collection and reporting to JDWNRH
- Provide guidance on isolates that should be sent for confirmatory testing to JDWNRH or RCDC reference centres
- Define the policies for long-term storage of representative isolates from the surveillance network in the bio repository at RCDC. This bio repository will be developed for future analysis of the mechanisms and genetic drivers of AMR
- Analyse and feedback AMR and AMU surveillance results to surveillance sites in collaboration with JDWNRH and RCDC

- Share and compare AMR and AMU surveillance results with the results from other sectors in the National AMR Technical Committee.
- Select a GLASS focal person to enrol Bhutan and share AMR data with WHO GLASS secretariat in Geneva
- Identify opportunities for collaborating with the animal health sector in training, equipment procurement and maintenance, purchase of reagents, etc.

The 3 proposed fellowships (laboratory, AMR and AMU surveillance) would provide leadership and technical support for the TWG (see Annex 2 for details).

The grant could provide support for the TWG by funding regular (e.g. quarterly) meetings to review progress in AMR and AMU surveillance, support the dissemination of documents and reports across the surveillance network and other AMR/AMU stakeholders.

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

- A MOH AMR and AMU surveillance TWG, with an agreed ToR, has met at least quarterly.
- All surveillance sites received revised national AMR standards and protocols
- Results from the TWG are presented to and discussed with the NATC.
- AMR and AMU surveillance results are regularly feedback to the surveillance sites
- Outputs and key AMR and AMU surveillance documents discussed during the meetings are stored (with back-ups) at the OH secretariat.
- Bhutan is fully enrolled with GLASS and, if possible, is sharing AMR data on a yearly basis

Output 2.2: Jigme Dorji Wangchuck National Referral Hospital (JDWNRH) is functioning as the clinical reference centre supporting the AMR surveillance system with a NATC-approved ToR

JDWNRH has been identified as the clinical reference center and will provide leadership and technical support for the laboratories in the surveillance network. JDWNRH will be the reference center for the priority pathogens other than enteric pathogens (see table 2 above). In addition to its role as the clinical laboratory of the hospital, the primary function of JDWNRH will be to promote good microbiological laboratory practice within the surveillance network, to serve as a resource and coordination point to harmonize laboratory testing and to maintain a central database of clinical and AMR data from all surveillance sites.

Possible areas to be validated by the NATC in a ToR for support by the Fleming Fund are described below:

- Participate in the revision of all laboratory related guidelines and quality documents led by the MOH TWG and assist in their dissemination
- Provide technical support and organise the training of the laboratory workforce to generate Quality Assured AMR data at surveillance sites (pathogen isolation, identification, AST & data entry using WHONET). Review and discuss External Quality Assessment (EQA) performances with laboratory managers at each surveillance site and provide corrective measures where appropriate.
- Provide confirmatory testing (pathogen ID at the species level, serotyping and resistance patterns) when needed or requested by surveillance sites
- Perform phenotypic characterisation of the mechanisms of AMR resistance on unusual resistance patterns from samples sent by surveillance sites

- Monitor Quality assurance at surveillance site through implementation of Quality Control procedures, training or refresher courses to clinicians in sample collection
- Participate in an international EQA scheme (EQAS) along with RCDC and animal reference laboratories
- Collect and quality assure the bacteriology and AMR data sent by surveillance sites each month
- Maintain a collection of routine and extended⁵ QC ATCC reference strains

JDWNRH is already conducting clinical bacteriology and providing AMR diagnostic services including Antibiotic Susceptibility Testing. A site assessment has shown that additional equipment and quality assured reagents have to be provided to improve the quality of services of the National Referral Hospital. In addition, diagnostic skills have to be strengthened to build the capacity in advance bacteriology and AMR: sub species level identification and phenotypic determination of the mechanisms of AMR. Beside equipment and direct laboratory support, the Grant could provide support and technical assistance to strengthen the activities of JDWNRH described above such as Train the Trainer courses of laboratory managers reviewing curriculum for trainings. Laboratory experts in AMR can provide advanced training and support to increase JDWNRH's expertise in bacteriology and mechanisms of AMR. By the end of the grant we expect that the following indicators will have been achieved:

A Laboratory Fellow at JDWNRH will significantly contribute to this output (see Annex 2 for details).

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

- JDWNRH is equipped to provide Quality Assured pathogen identification and AST following at least the list of national priority pathogens defined by the MOH AMR /AMU surveillance TWG
- JDWNRH delivers quality support services in bacteriology to its subordinate labs including training, Laboratory Quality Management documentation and confirmation of AMR diagnostic results.
- JDWNRH bacteriology laboratory personnel are trained in advanced techniques for pathogen identification and antibiotic resistance mechanisms characterisation
- Patient clinical information, Pathogen ID and AMR patterns from surveillance sites are collected, centralised and quality assured every month at JDWNRH for further epidemiological analysis by RCDC
- A collection of routine and extended QC ATCC strains is maintained.
- Microbiology laboratory personnel produce reliable confirmatory testing (identification and AST) as assessed by a relevant external quality assessment programme and by records of appropriate internal quality control.

Output 2.3: The Royal Centre for Disease Control (RCDC) is functioning as a reference centre for AMR in enteric pathogens and organise a biorepository with a NATC-approved ToR

The RCDC is currently isolating enteric pathogens (*E.coli*, *Salmonella* and *Shigella*) from stool sample collected and sent by surveillance sites as part of the disease outbreak surveillance mission of RCDC. RCDC will thus continue its role as a reference centre for enteric pathogens isolated from stool sample and play a key role in building the capacity at the surveillance sites whereby quality assured pathogens identification and AST is currently not available. RCDC will also lead the national External Quality Assessment program to monitor

⁵ Following EUCAST or CLSI international standard

quality within all surveillance sites. Possible areas for support by the Fleming Fund that will be validated by the NATC in a ToR are described below:

- Participate in the revision of all laboratory related guidelines and quality documents led by the MOH TWG and assist in their dissemination
- Act as the reference centre for enteric pathogens by:
 - provide technical support and trainings at surveillance site for correct isolation, identification and AMR testing of *E.coli*, *Salmonella* spp and *Shigella* spp from stool sample
 - Advanced identification of *Salmonella* spp and *Shigella* spp species by serotyping
 - Perform phenotypic characterisation of the mechanisms of AMR resistance present in enteric pathogens
- Organise and lead the External Quality Assessment Programme on AMR to monitor quality at surveillance sites by sending every month at least one blind sample to be identified and test for antibiotic susceptibility. RCDC will collect and analyse EQA data to inform JDWNRH on correctives measures to implement locally or at the national level (SOP revisions if needed)
- Implement a secure, inventoried, biorepository following MOH TWG guidance (e.g. selection of isolates for saving, arrangement for accessing isolates, etc. see output 2.1 above)
- In charge of the automated or semi-automated bacteriology ID and AST platform for MIC testing for all AMR surveillance sectors (Human, Animal and Food)
- Perform advanced testing on AMR resistance (MIC and PCR) for priority pathogens for epidemiological purposes
- Assist JDWNRH in training and capacity building at surveillance sites with a focus on enteric pathogens
- Participate in an international EQA along with JDWNRH and animal and food reference laboratories

As for JDWNRH, laboratory capacity assessment has shown that additional equipment and quality assured reagents have to be provided to match the missions of the centre. the Fleming Fund Country Grant can support RCDC by providing international Technical Assistance for refresher trainings on advance pathogen identification and sub species characterisation using serological testing, phenotypic or genotypic (PCR) characterisation of the mechanism of AMR resistance and other support to strengthen the centre and the proposed activities. By the end of the grant we expect that the following indicators will have been achieved at RCDC:

- RCDC is equipped to culture, identify and conduct AST on enteric pathogen as defined by the MOH AMR /AMU surveillance TWG
- RCDC bacteriology laboratory personnel are trained in advanced techniques for pathogen identification and antibiotic resistance mechanisms characterisation phenotypically
- An inventoried national biorepository of bacterial isolates from all surveillance laboratory in the public health sector is securely maintained.
- A national EQA is in place allowing regular improvement of the Quality of AMR testing
- RCDC is in capacity to provide a service of MIC determination for the different AMR surveillance sectors following procurement of an automated or semi-automated system selected by the NATC in collaboration with IPA and the Managing Agent

- Microbiology laboratory personnel produce reliable confirmatory testing (identification and AST) as assessed by a relevant external quality assessment programme and by records of appropriate internal quality control.

Output 2.4: The bacteriology laboratories at Gelephu Regional Referral Hospital, Mongar Regional Referral Hospital and Phuentsholing General Hospital generate quality assured AMR data

During the preparation of this RFP, assessments of the capacity to conduct and share quality AMR surveillance data have been conducted at each surveillance site. These site visits identified the following needs that have to be addressed in laboratory renovation, equipment, trainings and capacity building:

- Link the laboratory data with the Health Management and Information System (HMIS; see below output 2.7) for smooth integration of relevant clinical information and AMR data for sharing with the reference center
- In collaboration with IPA provide and install the equipment for safe and secure quality AMR testing as per the procurement plan
- Ensure that quality assured reagents are provided at each site
- Provide training or refresher course in sample collection (at least blood and urine and stool) to clinical and laboratory staff to reduce contamination rate
- Review laboratory procedures and quality controls following the recommendations and guidelines established by the MOH TWG
- Support the training programme in pathogen isolation, identification and routine AST developed by JDWNRH & RCDC

To ensure that surveillance sites are in capacity to provide and share quality assured AMR data with the reference centre the grantee can mobilise technical assistance specialised in IT infrastructure in hospital settings, assist in supporting trainings or workshop and work with IPA for effective laboratory renovation. By the end of the Grant we expect that the following indicators will have been achieved:

- QC for laboratory tests developed by the MOH TWG and the reference centres are in operation at each surveillance sites. In particular routine QC reference strains are used when measuring AST and sheep blood is always used for preparing Blood-Agar plates
- An up-to-date CLSI or EUCAST standard (depending on which standard will be selected by the MOH TWG) is followed and properly used by all laboratory personnel
- Use of quality brands of reagents and antibiotic disks according to international reference organization (CLSI/EUCAST)
- Contamination rate of blood culture is measured and below 5%.
- The surveillance sites are regularly participating in the national EQA programme established by the RCDC and achieve satisfactory results.
- Additional indicators developed by the MOH TWG

Output 2.5: Biosafety and biosecurity measures are in place at reference centers, surveillance sites and for the transportation of samples and strains within the network

Biosafety and biosecurity measures across the different component of the surveillance network have to be improved to develop a safe and secure AMR surveillance system. Needs have been identified during site assessment allowing the Grantee to develop specific and tailored activities in collaboration with IPA.

- Procure and install all necessary biosafety equipment as identified during site visits (Biosafety cabinets, autoclaves etc.)
- Ensure secure and restricted access to the bacteriology laboratory and storage facility (bio repository) to contain the spread of resistance pathogens
- Develop the procedures for safe and secure transportation of QC strains to surveillance sites and transportation of isolates for confirmatory testing and long-term storage in the biorepository at reference centres. Train personnel and sub-contractors involved in transportation of infectious substances material following international regulation⁶
- Train clinicians and laboratory personnel and any other actors in the surveillance system in Biosafety and Biosecurity

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

- All laboratories are equipped to reach BSL2 with functional safety equipment (BSCs) and personal protective equipment (refer to CDC BMBL 5th edition⁷)
- Safe and secure transportation of infectious substances is organised within the surveillance system according to the needs
- Clinical, laboratory and subcontractors are trained in Biosafety and Biosecurity adapted to the level of exposure to pathogens or activities

Output 2.6: Surveillance sites are regularly sending quality AMR, clinical and basic epidemiological data to JDWNRH

AMR data is currently shared with JDWNRH on a yearly basis which do not (a) provide the necessary feedback control mechanism to identify potential issues in the quality of the AMR diagnostics generated at surveillance sites and (b) is not sufficient to generate meaningful information for epidemiological analysis of AMR data locally or at the national level. In addition, lack of operational HMIS system in hospitals (including the reference lab) affects the collection of clinical and basic epidemiological data as recommended by GLASS. The Fleming Fund could thus support the activities described below:

- Implement a computerized Health Management and Information System (HMIS) at the hospitals to collect basic patient and epidemiological data relevant at least for AMR surveillance
- Link AMR collected data using WHONET to the HMIS
- Train hospital personnel in and basic epidemiological data collection as determined by the MOH AMR surveillance TWG
- Provide refresher courses on AMR data collection using WHONET to all laboratory staff involved in bacteriology and AST

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

- Each surveillance site is regularly (at least monthly) sending consolidated clinical epidemiological and laboratory data to JDWNRH for each sample that enters the surveillance of AMR

⁶ WHO Guidance on regulations for the **Transport of Infectious Substances** 2015–2016 – WHO/HSE/GCR/2015.2

⁷ Biosafety in Microbiological and Biomedical Laboratories 5th Edition – HHS Publication No. (CDC) 21-1112 – Revised December 2009

Output 2.7: Quarterly and annual reports of AMR and AMU surveillance results are shared with the MoH AMR and AMU Surveillance TWG, the NATC and the surveillance sites

AMR data is only analysed on a regular basis for enteric pathogens from stool sample by the RCDC. Regular collection of AMR data on all national priority pathogens isolated from the priority specimen by JDWNRH should thus be strengthened to increase in overall capacity to analyse AMR data from the surveillance network. In addition to the technical support for enteric pathogens (see above output 2.3) the RCDC through its epidemiology unit will be involved in AMR data analysis that has been quality assured by JDWNRH. These analyses should then be shared with the OH AMR /AMU TWG surveillance.

- Provide equipment and IT support to organise the clinical and AMR database at RCDC and provide appropriate training in database management
- Technical Assistance to build the capacity to analyse AMR data including basic statistical description of the data, epidemiological interpretation

AMR and AMU Surveillance Fellows will significantly contribute to this output (see Annex 2 for details).

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

- Epidemiologists at RCDC are trained to analyse AMR data collected from surveillance sites by JDWNRH
- RCDC is sending nationally collated resistance data on priority pathogens to the surveillance site
- RCDC epidemiology unit produces a report showing the results from analyses of the AMR surveillance data every 4 months and shares the results with OH AMR and AMU Surveillance TWG

Output 2.8: Capacity and needs assessment completed for 3 additional surveillance sites using the Fleming Fund site assessment tool

3 additional surveillance sites, Tashigang Hospital, Samtse Hospital and Samdrupjongkhar Hospital will be evaluated to prepare the expansion of the surveillance system in Bhutan. Local assessors have already been trained to assess laboratory capacity and needs using the Public Health Site Assessment tool specifically developed for the Fleming Fund Country Grant. Logistic support organised by the selected Grantee will be required to reach these sites

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

- Needs assessment at 3 additional surveillance sites

Output 2.9: At least 3 biomedical engineers from the Department of Medical supplies & health services/MOH are trained and accredited

Lack of trained and certified biomedical engineers to maintain equipment for Quality Assured bacteriology and Resistance data collection. Training of additional biomedical engineers at the Department of Medical supplies & health services

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

- 3 certified biomedical engineers able to provide technical and maintenance support for the microbiology laboratories in Human Food and animal AMR surveillance

10.3 Objective 3: Strengthen AMR and AMU surveillance in food animals

The focus of AMR surveillance in food animals supported by the first country grant will be on testing for resistance in enteric bacteria in healthy broilers and layer hens at NCAH and RLDCs of Chukha and Trashigang. It will also include the National Food Testing Laboratory (NFTL) to test for resistance in bacteria on locally grown chicken in the Thimphu area.

Table 3. Sampling plan for AMR surveillance in broilers and layer hens.

Poultry Sector	# samples /lab/year	Total #/3 labs/year	Samples per farm	Sampling location
Broilers	130-135	400	Caecal samples from 5 birds, pooled into 1 sample 10 farms sampled every 2 weeks	Slaughterhouse
Spent layer hens	130 - 135	400	Cloacal samples from 5 birds, pooled into 1 sample (Collect caecal samples if possible) 10 farms sampled every 2 weeks	Layer farm

Table 4: The target bacteria and antibiotics are:

Category	Name	Location
Clinical Reference Lab	Jigme Dorji Wangchuck National Referral Hospital (JDWNRH)	Thimphu
Epidemiology Reference Lab	Royal Centre for Disease Control (RCDC)	Thimphu
Surveillance site	Gelephu Regional Referral Hospital	Gelephu
Surveillance site	Regional Referral Hospital	Mongar
Surveillance site	Phuentsoling General Hospital	Phuentsoling

	Bacteria	Laboratory	Antibiotics
GLASS priority pathogens	<i>Escherichia coli</i>	All labs	
	<i>Klebsiella pneumoniae</i>		
	<i>Salmonella spp</i>		
Additional zoonotic pathogens/indicators	<i>Campylobacter spp</i>	NVL (NCAH), NFTL	
	<i>Enterococci</i>	All labs	
	<i>(E. faecium and E. faecalis)</i>		

Output 3.1: A MOAF AMR and AMU Surveillance TWG functioning in accordance with an approved ToR

In addition to the MOAF-appointed AMR focal point, there is a need for a multi-disciplinary technical working group (TWG) to lead AMR and AMU surveillance in animals and food. Membership of the group could expand as the coverage of surveillance is expanded in the future, e.g. to include the environment and Department of Agriculture.

The TWG would be chaired by the Chief Veterinary Officer (CVO) of Department of Livestock. Suggested membership of the TWG would comprise the MOAF AMR focal point, Director of the National Veterinary laboratory, NCAH epidemiologist responsible for analysing AMR surveillance data, food microbiologist from NFTL and representative from the veterinary drug committee.

The 3 proposed animal health fellowships (laboratory, AMR and AMU surveillance) would provide leadership and technical support for the TWG, together with other technical leaders working in this area (see Annex 2 for details).

Suggested roles of the TWG are:

- Provide technical input to the design and support implementation of AMR and AMU surveillance in animals and food.
- Discuss and interpret AMR and AMU surveillance results.
- Understand what the surveillance results contribute to knowledge about AMR & the links between AMU and AMR in animals and people in Bhutan.
- Identify priorities for further surveillance and/or investigations.
- Maintain a repository of the outputs from AMR and AMU surveillance in animals and food.
- Share and compare animal AMR and AMU surveillance results with the results from other sectors in the National AMR Technical Committee.
- Identify opportunities for collaborating with the human health sector in training, equipment procurement and maintenance, purchase of reagents, etc.

The grant could provide support for the TWG by funding regular (e.g. quarterly) meetings of the TWG to review progress in AMR and AMU surveillance.

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

- A MOAF AMR and AMU surveillance TWG, with an agreed ToR, has met at least quarterly.
- Reports and key AMR and AMU surveillance documents discussed during the meetings are stored (with back-ups) by the AMR focal point.
- Results from the TWG are presented to and discussed with the NATC.

Output 3.2: National Veterinary Laboratory (NVL) is functioning as a reference laboratory

The National Veterinary Laboratory (NVL) in the National Centre for Animal Health has been identified as the national AMR reference laboratory for animals and food. The NVL will provide leadership and technical support for the laboratories in the two Regional Livestock Development Centres that are participating in the surveillance network and the NFTL. The NVL already runs diagnostic training and has produced an SOP for microbiology and AST. However, the SOP needs to be upgraded to include all the organisms included in the AMR surveillance. The country grant can provide support for the NVL to undertake the following in its role as reference laboratory:

- Train and mentor microbiology technicians in RLDCs and NFTL in culture, identification and AST methods.
- Maintain quality diagnostic systems in AMR surveillance labs
 - Coordinate production of bench guides/flow charts
 - Upgrade current SOP to include all the bacteria in the surveillance programme
 - Training/mentoring on QC and IQAS
 - EQAS amongst AMR surveillance labs
- Maintain an inventoried national biorepository of isolates produced by all labs in the surveillance network.
- Maintain an ATCC strain collection.
- Collate & verify AMR surveillance diagnostic data from the contributing labs
- Participate in an international EQAS
- Develop the capability to undertake the following more advanced diagnostic methods:
 - ESBL-, acquired AmpC (pAmpC) and/or carbapenemase-producing organism confirmation
 - *Salmonella* spp serotyping
 - Minimum Inhibitory Concentration (MIC) tests on a subset of isolates showing resistance on disk diffusion tests to identify epidemiology cut-off values (ECOFF) which ensures the comparability of data over time at the country level and also facilitates the comparison of resistance patterns between countries.

A Laboratory Fellowship based in the NVL, NCAH will significantly contribute to this output (see Annex 2 for details).

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

- Updated SOP for culture, identification and AST of all the bacteria included in the AMR surveillance programme is being used in all the microbiology laboratories in the surveillance programme.
- NVL has run at least 1 workshop to train microbiology technicians from the participating labs in culture, identification and AST.
- An inventoried national biorepository of bacterial isolates from all labs is securely maintained at NVL.
- A collection of all the necessary ATCC strains is maintained at NVL.
- A national database of verified AMR data is maintained by NVL using WHONET.
- NVL runs an IQAS with the labs participating in the AMR surveillance programme.
- NVL achieves satisfactory results in an international EQAS.
- NVL has the capability to conduct phenotypic testing to confirm ESBL-, acquired AmpC and/or carbapenemase-producing pathogens.
- NVL has the capability to serotype the major *Salmonella* species found in animals.
- NVL has conducted MIC tests on a representative sample of isolates that showed some resistance on disk diffusion to obtain ECOFF values.

Output 3.3: NVL, Chukha RLDC lab, Trashigang RLDC lab and the National Food Testing Laboratory produce reliable quality bacterial culture, identification and Antibiotic Susceptibility Testing (AST) results for *E. coli*, *Klebsiella*, *Salmonella* spp and Enterococci.

Laboratories in the RLDCs have the capability to culture and identify the priority organisms identified for AMR surveillance. They have experience conducting antibiotic susceptibility testing (AST). However, the diagnostic skills need to be strengthened across all the labs participating in the surveillance system, using reliable quality antibiotic disks and media.

NFTL has ISO/IEC 17025:2005 accreditation for culture and identification of *Salmonella* spp, *E. coli*, *Staphylococcus*, *Bacillus cereus*, Total Plate Count, Yeast and Mould Count, and coliform. However, the lab has no experience with AST.

NVL has capability to culture, identify and conduct AST on the priority organisms.

However, in all labs the quality of antibiotic disks and of media is not sufficient and in some cases stock is past its expiry date.

Specific renovation and equipment needs for each lab have been identified and are listed in a separate procurement list.

The IPA will procure and install the equipment that is required by each lab for quality microbiology testing.

The Grantee will need to organise servicing of equipment.

Microbiology technicians in the participating labs need training in culture, identification and AST for the organisms that are included in the AMR surveillance programme.

NVL will support the other labs in implementing good quality systems and will run an EQAS involving the surveillance labs.

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

- All labs have the necessary equipment to 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 the SOPs.

Output 3.4: NVL and NFTL have the capacity to culture *Campylobacter* spp

This is an important zoonotic pathogen of humans that is carried by animals and which can also cause disease in animals. It is identified by WHO as a priority bacterium with respect to growing antibiotic resistance, especially to fluoroquinolones.

The NVL and RVL staff have the skills to culture and identify all the priority bacteria for the AMR surveillance programme, other than *Campylobacter*. This programme provides a good opportunity to strengthen the capability of the vet labs and NFTL to culture *Campylobacter*, beginning with CVL who could then train and support RVL staff.

The labs have candle jars and need gas packs to create the microaerophilic culturing environment.

RCDC has capability to grow *Campylobacter* spp and can provide training and on-going mentoring to the NVL and NFTL to develop capability accurately grow *Campylobacter*.

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

- NVL and NFTL will be accurately culturing *Campylobacter* species.
- RCDC will periodically test accuracy of *Campylobacter* culturing capability in NVL and NFTL.

Output 3.5: Biosafety and biosecurity measures are being applied within NVL, the two RLDC laboratories and the NFTL and to the safe transport of samples and isolates between the laboratories

The NVL should review biosafety and biosecurity across the four labs in the AMR surveillance programme at the beginning of the Grant period to identify the biosafety and biosecurity issues that need to be addressed in each lab.

Training should be provided to lab staff and on-going audits conducted to ensure adequate biosafety and biosecurity.

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

- The labs are 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 in all labs.
- All waste is disposed of in a safe manner.
- Isolates are transported in a safe manner between laboratories.

Output 3.6: Good quality samples from healthy layer hens and broilers are regularly sent to NVL, CRVL and WRVL for culture and AST, according to the agreed schedule.

A SOP for collecting samples should be prepared at the beginning of the grant period, if not already available, and sample collectors trained.

Good quality reagents and consumables need to be purchased for sample collection and transport.

Costs of sample collection need to be covered under the Grant i.e. transport costs.

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

- RLDC staff collect appropriate samples for AMR testing that are labelled appropriately, transported in a safe manner, arrive at the laboratory in good condition for diagnostic testing, and are accompanied by appropriate demographic information that is labelled to match the samples.
- Staff from the 3 centres included in the AMR surveillance programme have sent approximately 135 samples to their laboratory for AMR testing.

Output 3.7: Good quality samples from locally grown chicken meat are regularly sent from meat shops in Thimphu to NFTL for culture and AST, according to the agreed schedule

A sampling plan needs to be designed at the beginning of the grant period to collect 400 samples from locally produced chicken in meat shops in Thimphu over the grant period. If possible the source of the chickens should be identified when sampling, and only 1 carcass sampled per source location at any one time.

A SOP for collecting samples should also be prepared at the beginning of the grant period, if not already available, and sample collectors trained.

Good quality reagents and consumables need to be purchased for sample collection and transport.

Costs of sample collection need to be covered under the Grant i.e. transport costs.

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

- A SOP has been prepared for collecting chicken carcass samples and submitting to the NFTL.
- Approximately 400 locally produced chicken carcass samples from Thimphu meat shops have arrived at the NFTL in good quality for AMR testing.

Output 3.8: A national database of verified AMR results and associated demographic data is maintained in WHONET at the NVL

NVL currently has a version of WHONET that is customised for Bhutan. WHONET is not yet installed in RLDCs or the NFTL. The NVL version of the software can be distributed to the laboratories in the RLDCs and NFTL and training provided for staff in each lab to enter the AMR results, including AST results and correctly matched demographic data. A computer, printer and USP will need to be purchased for each lab to maintain the WHONET database.

Each lab would be responsible for maintaining an accurate database of the samples that they test for AMR and would send a monthly dataset to NVL for updating the national AMR database.

Results from AST conducted on clinical animal samples should also be entered into the database as well as those collected for AMR surveillance in healthy birds so that AMR associated with animal illness is also analysed.

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

- Each lab maintains a WHONET database with results for all samples tested under the surveillance programme accurately matched to demographic details for each sample.
- WHONET database is regularly backed up in each lab.
- NVL maintains a national WHONET database including verified results from all participating labs, which is also regularly backed up.

Output 3.9: NCAH shares quarterly and annual reports of AMR and AMU surveillance results with the MOAF AMR and AMU Surveillance TWG, the NATC and the RLDCs

The Disease Prevention and Control Unit of NCAH, which contains epidemiology expertise, will be responsible for epidemiological analysis of the data collected through AMR surveillance.

NVL should send the WHONET AMR database to NCAH every three months for analysis.

Analysis and interpretation of the AMR surveillance data will be supported by a Fleming Fellowship (see Annex 2 for details). Hence there are minimal requirements for the country grant to support this aspect of the programme.

The AMR results should be interpreted in the context of data collected on AMU in the surveillance populations.

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

- NCAH epidemiology unit produces a report showing the results from analyses of the AMR surveillance data every 6 months and shares the results with MOAF AMR and AMU Surveillance TWG, NFTL and the RLDCs.
- Results of AMR surveillance are interpreted in the context of AMU surveillance data.

Output 3.10: G2C extended database for electronically recording prescription and antibiotic use data in veterinary districts is recommended.

The Veterinary Drug Committee in the NCAH is responsible for managing antibiotics used by the animal health services in Bhutan. A national veterinary drug database is about to be launched. The database, developed through the G2C programme will act as inventory management for veterinary drugs, between the central warehouse and the RLDCs.

Paper-based records on antibiotic prescriptions are maintained in the veterinary districts.

Private people have recently been registered to use antibiotics, including some farmers and private pharmacies.

A Fleming AMU/C surveillance Fellowship will analyse national veterinary antibiotic records and support reporting AMC data to OIE. It will also analyse AMU data that is currently stored in paper records, in either one or both of the Chukha and Trashigang RLDCs, also including antibiotics used by private pharmacies. AMU data will be transferred from paper records to an electronic database for data analysis. An outcome of the Fellowship will be recommendations on the design of an electronic database for recording antibiotic prescription data.

The Country grant will cover the following:

- Training in use of G2C database for management of veterinary drugs.

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

- All staff in RLDCs are trained in using the G2C database.
- A set of recommendations on how to extend the G2C database to include recording of veterinary prescription data. (Note: The IT costs of extending the G2C database could be covered in the second country grant).

11 Annex 2: Possible Fleming Fellowships in Bhutan

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic expertise	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Human	AMR Surveillance	RCDC	<p>Keep up to date with all the available information on AMR and AMU in Bhutan</p> <p>Understand the likely AMR mechanisms in Bhutan</p>	Contribute to designing future targeted AMR surveillance			<p>Collate and analyse existing AMR data (outbreak investigations)</p> <p>Analyse AMR surveillance data</p> <p>Understand data biases</p> <p>Interpret AMR results in consultation with microbiologist and AMU data</p>	<p>Discuss AMR and AMU results from human and animals</p> <p>Present overall understanding of AMR in Bhutan</p>	To be discussed at the time of agreeing on the Fellowship workplans
Human	Laboratory	JDWNRH	<p>Keep up to date with all the available information on AMR and AMU in Bhutan</p> <p>Understand the likely AMR mechanisms in Bhutan</p>		Phenotypic testing for resistance (ESBL, acquired AmpC (pAmpC) and/or carbapenem resistance)	Improve quality of culture, identification and AST in surveillance site laboratories		<p>Discuss AMR and AMU results from humans and animals</p> <p>Present AMR results from humans (with AMR Surveillance Fellow)</p>	To be discussed at the time of agreeing on the Fellowship workplans

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic expertise	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Human	AMU Surveillance	JDWNRH	<p>Keep up to date with all the available information on AMR and AMU in Bhutan</p> <p>Understand the likely AMR mechanisms in Bhutan</p>				<p>Conduct survey of prescribing practices in JDWNRH</p> <p>Analyse and interpret AMU surveillance results</p> <p>Work with clinicians to modify prescribing practices to reduce potential for AMR</p>	<p>Discuss AMR and AMU results from human and animals</p> <p>Present AMU results from humans so that AMR results are related to AMU patterns</p>	To be discussed at the time of agreeing on the Fellowship workplans

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic expertise	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Human	AMC surveillance	JDWNRH	Keep up to date with all the available information on Antibiotic distribution at public healthcare facilities in Bhutan				<p>Develop a data collection survey based on ATC/DDD methodology</p> <p>Collate and analyse existing ATC/DDD data from a selection of surveillance sites</p> <p>An outcome of the Fellowship will be recommendations on the design of an electronic database for recording antibiotic consumption data at Hospital pharmacies</p>	<p>Present stratified AMC data from selected surveillance site pharmacies</p> <p>Discuss AMU and AMR data from human and animals</p>	To be discussed at the time of agreeing on the Fellowship workplans

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic expertise	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Animal	Laboratory	NVL, NCAH	<p>Keep up to date with all the available information on AMR and AMU in Bhutan</p> <p>Understand the likely AMR mechanisms in Bhutan</p>		<p>Phenotypic testing for resistance (ESBL, acquired AmpC (pAmpC) and/or carbapenem resistance)</p> <p>Minimum Inhibitory Concentration testing for antibiotic resistance</p>	<p>Improve quality of culture, identification and AST in regional laboratories</p>		<p>Discuss AMR and AMU results from human and animals</p> <p>Present AMR results from animals (with Surveillance Fellow)</p>	<p>To be discussed at the time of agreeing on the Fellowship workplans</p>
Animal	AMR Surveillance	NCAH	<p>Keep up to date with all the available information on AMR and AMU in Bhutan</p> <p>Understand the likely AMR mechanisms in Bhutan</p>	<p>Contribute to designing future targeted AMR surveillance</p>			<p>Collate and analyse existing AMR data (clinical cases)</p> <p>Analyse AMR surveillance data</p> <p>Understand data biases</p> <p>Interpret AMR results in consultation with microbiologist and AMU data</p>	<p>Discuss AMR and AMU results from human and animals</p> <p>Present AMR results from animals (with Lab Fellow)</p>	<p>To be discussed at the time of agreeing on the Fellowship workplans</p>

Sector	Fellowship	Beneficiary Institution	Understanding AMR	Surveillance expertise	Diagnostic expertise	Lab quality management systems	Data collection, analysis and use	OH Technical working group	Collaborative project
Animal	AMC/U Surveillance	NCAH	<p>Keep up to date with all the available information on AMR and AMU in Bhutan</p> <p>Understand the likely AMR mechanisms in Bhutan</p>				<p>Analyse national veterinary antibiotic records and support reporting AMC data to OIE.</p> <p>Analyse AMU data that is currently stored in paper records, in either one or both of the Chukha and Trashigang RLDCs, also including antibiotics used by private pharmacies.</p> <p>AMU data will be transferred from paper records to an electronic database for data analysis. An outcome of the Fellowship will be recommendations on the design of an electronic database for recording antibiotic prescription data.</p>	<p>Discuss AMR and AMU results from human and animals</p> <p>Present AMC and AMU results from animals</p>	