Terms of Reference for Regional Grants round 1

1.1 Overview

Regional Grants will be funded by UK Department of Health under its Fleming Fund Grants Programme. The aim of the Fleming Fund is to address critical gaps in surveillance of antibiotic resistance 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 antimicrobial resistant (AMR) infections. Led by the UK, political action against the problem has resulted in a roadmap for global response - the Global Action Plan on Antimicrobial Resistance (AMR)[1]. This is the blueprint for a multi-stakeholder global response to averting the burden of AMR. Mott MacDonald has been appointed as the Fleming Fund Management Agent and is responsible for the management of the Fleming Fund Grants Programme.

The Fleming Fund Grants Programme includes Regional Grants in each of the four Fleming Fund regions (West Africa, East and Southern Africa, South Asia and South East Asia), offering four grants in this round 1. This Regional Grants round 1 is a "call for data" which aims to expand the volume of historical and current data available on AMR and AMU across regions. Regional Grants round 2 is planned for later in 2018 and aims to support Country Grants by enhancing regional coordination and collaboration across quality assurance and quality control, regional data sharing, regional responses, and human resource and laboratory capacity building.

A Lead Grantee for each Regional Grant will need to work in close coordination with the Management Agent and to harmonise the proposal with other types of grants under the Fleming Fund Grant Programme being the Country Grants and the Fleming Fellowship Scheme, and with national stakeholders in countries where the Lead Grantee will operate.

Regional Grant Round I is expected to last 18-24 months. Potential applicants will need to contact the regional hub of the Management Agent to register their interest and then, subject to suitability, be invited to apply using an Expression of Interest.

1.2 Overview of the Fleming Fund

1.2.1 Introduction

The UK Government has established the Fleming Fund to respond to the global threat of antimicrobial resistance (AMR). The Fleming Fund is critical to 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 UNGA on Antimicrobial Resistance, 2016'. These initiatives recognise that urgent cross sectoral rationalisation of antimicrobial use (AMU) 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 aim of the Fleming Fund Grants Programme is to improve the ability of recipient countries and regions to improve surveillance and monitoring of AMR. This includes enhancing diagnosis of drug resistant infections, with an emphasis on antibiotics and priority bacterial diseases, improving the monitoring of antimicrobial

[1] http://www.wpro.who.int/entity/drug_resistance/resources/global_action_plan_eng.pdf

usage, and improve data quality and volume to inform policy and practice at national and international levels. The goal is to avert the human and economic burden of antimicrobial resistance.

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

The geographic focus of the Fleming Fund Grants Programme is low and lower-middle-income countries in four regions: West Africa, East and Southern Africa, South Asia and South East Asia. It provides financial support to participating countries via three funding channels, over a five-year period from 2017 to 2021:

- Country Grants
- Fleming Fellowship Scheme, that provides continual professional development and leadership training opportunities for relevant fellows
- Regional Grants

In subsequent Requests for Proposals, resources may also be made 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 adaption purposes.

The UK Department of Health 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 allocating funding and oversight of all investments made across the Fleming Fund Grants Programme. The Fleming Fund Grants Programme will be independently evaluated and Itad, a specialist evaluation firm, has been appointed for this purpose.

1.2.2 Problem statement to be addressed by the Fleming Fund at the regional level

There are too few datasets to support evidence based policy and treatment, and to enhance appropriate use of antibiotics in LMICs. This lack of data is outlined in recent publications[2]. Although efforts to improve the quality and volume of data are being made, resources are required to improve the collection and collation of data, and to set baselines for specific priority drug/bug combinations outlined in the GLASS manual and the LSHTM roadmap, and that address local AMU. In addition, little information exists on resistance patterns against commonly used standard (and non-standard) treatments or those used in agriculture.

However, there are, in most countries, institutions (academic, research, public and private health facilities, etc) which have been collecting data on AMR, sometimes for decades. This 'hidden treasure' data is simply inaccessible for use in large-scale analytics. Collecting and, where necessary, digitalising data from these institutions has the potential to provide a synergistic analytical power to undertake analysis of spatiotemporal

[2] World Health Organization: Worldwide country situation analysis: response to antimicrobial resistance. 2015. WHO/HSE/PED/AIP/2015.1 http://apps.who.int/iris/bitstream/10665/163468/1/9789241564946_eng.pdf?ua=1&ua=1

trends and establish baselines of AMR across a wide range of pathogen/drug combinations. Likewise retrieving data on antimicrobial use through prescription data or volume of antibiotic consumption in healthcare facilities should provide a wealth of information for baseline data on AMU and potential drivers of AMR (at least for healthcare associated infection). This Regional Grants round 1 will therefore focus (though not exclusively) on:

- The GLASS priority pathogens, but will also encompass a wider group of bacterial pathogens of local interest to human health whether or nor not a surveillance system of AMR is active in a region or country.
- AMR data of critically important antimicrobials (see the GLASS list of pathogen–antimicrobial combinations and WHO CIA list 5th revision 2017), and evidence of resistance mechanism (for example, ESBL).
- Antimicrobial Use in public health settings either from drug consumption data from hospital pharmacies or prescription data issued by physicians and other prescribers.

The aims of the Regional Grants round 1 are to:

- Increase the volume of data available to improve spatiotemporal mapping of AMR and AMU across countries in each region, thus providing baseline data.
- Assess the quality of each dataset and provide meta-data to give regional and inter-regional context.
- Collect retrospective data from multiple sources in the public and private human healthcare sector, research and surveillance. This can include industry-led initiatives.
- Undertake analysis of the data and ensure it is disseminated locally, regionally and globally using appropriate platforms (e.g. online, peer reviewed publications).
- Improve local capacity to collect and use data at the national, regional, and global level by partnering with local institutions, including national Governments.
- Identify gaps in data from regions, considering whether this is as a result of low volumes of diagnostic testing or due to a lack of reporting of data.
- Identify areas of quality improvement and acknowledge issues with data interpretation that can be addressed in future standardisation of surveillance.
- Assist in improving awareness, advocacy and policy with a view to addressing the problem of AMR and AMU at the country and regional level.

1.3 Description of tasks

1.3.1 Develop a plan to collect past and present AMR and AMU data

The plan should include:

- A list of healthcare institutions and organisations operating in the region where past and present data will be collected, and the approach used to find additional sources of data during the course of the grant. The Managing Agent's Regional Coordinator will provide an initial list in their specific region, although it should not be the sole source for the selection of institutions. It is expected that the Lead Grantee will have outstanding networks and knowledge of the landscape in the region(s) for which they are applying.
- Inclusion and exclusion criteria for the selection of participating institutions taking into consideration a net as wide as possible for subsequent assessment of the regional distribution of data, irrespective of quality or amount of the data.

- The composition of the team involved in data collection (include CVs of the Project Leader and key staff members).
- A timeframe and budget for the data collection in the region.

The grantee will work with national governments, academic institutions, Non-governmental Organisations and other partners involved in AMR monitoring and treatment from the region to acquire data. Some countries and organisations are not enrolled or have not yet shared AMR data into GLASS. The grantee will thus need to assess the tolerance for data sharing by focus countries and institutions, identify participants, champions and future co-authors to ensure that intellectual property issues are properly addressed. The grantee should develop Data Transfer Agreements with contributing institutions and should enable open access to the data, including sharing with other global initiates (such as the Global Burden of Disease survey by the Institute for Health Metrics and Evaluation).

1.3.2 Develop a grading system to rate the level of the quality of AMR and AMU data

The quality of the AMR data (and to a lesser extent AMU data) is likely to be variable and is highly dependent on the level of development, quality management systems and skills at a given diagnostic facility or organisation. The Lead Grantee will first propose a rating system to assess the quality and quantity of the AMR and AMU data collected. For alignment purposes among the four regions, a final grading system will be discussed during a workshop between the selected Lead Grantees and the Management Agent using the contribution from each selected grantee.

1.3.3 Undertake data retrieval activities in the region

The goal of this Regional Grant round 1 is to enlarge the body of data available locally, regionally and globally by including unreported data, so it does not need to include data or information from published articles, meta-analysis or other information in the literature. Potential data sources are raw data from clinical microbiology laboratories (e.g. isolate identification, % resistance), primary clinical data of bacterial infection and treatment, and grey literature (e.g. unpublished research data). The data that will be considered are:

- **Microbiology data:** outcomes of diagnostic tests on bacterial species and antimicrobial resistance focusing on the GLASS list of priority pathogens, but also including other locally important bacterial species.
- **Resistance patterns** and data on mechanisms of resistance (e.g. ESBLs, carbapenamases).
- **Clinical and epidemiological data** associated with samples, for example exposure data, clinical signs and symptoms, treatments prescribed, and clinical outcomes (where available).
- Data on **antibiotic consumption** (1st line and 2nd line treatment) from the facility and treatment outcome when available and/or prescription data when available including those commonly used locally (e.g. in local treatment guidelines).
- **Prevalence survey data** of pathogens and resistant pathogens and genes in healthcare settings and/or healthy populations (e.g. community carriage).
- **Genotype/whole genome sequence data:** Any associated genotype/sequence data from isolates or laboratory records should be included, where relevant and appropriate. This may include information on genetic background, virulence and resistance markers.
- **Geo-location data:** Location data for each site, or, where available, individual specimens, to allow geo-spatial analysis.

The data will be gathered in sequential order of priority:

- Primary level: AMR and AMU from anonymised line-listing samples.

And if not available:

- Secondary level: corresponding to aggregated data by syndrome, species (if available), and drug/bug combination (c.f. GLASS).

And if not available:

- Tertiary level: capabilities and description of the metadata for a dataset that might be available and describe why the data could not be shared.

1.3.4 Develop an analytical model to be used for each type and grade of data

The analytical plan should be appropriate to the data quality, and take full account of the limitations in the data. The analysis should be as robust as possible with due regard to the underlying quality and statistical power. Where possible it should include spatiotemporal analysis. To allow comparability, analytical models will be presented and discussed during a workshop to share and refine similar (or the same) model(s) across regions.

Where epidemiological data is available to accompany laboratory data, this should be analysed with appropriate explanatory variables using pre-defined analysis plan. Key data might include person, place, time (PPT) data, clinical outcomes (e.g. day 7 outcome), and other exposure data (such as occupational risk).

1.3.5 Analyse AMR and AMU data in the region

- The Lead Grantee will ensure analysis of the data for that region to generate a baseline stratified by pathogens, antimicrobials and other markers (e.g. genotype data) as specified by the analytical models.
- Produce spatiotemporal heat maps to link AMR/AMU data with population density, catchment area, density and type of healthcare structures and other relevant socio-demographic markers. Precise models of dissemination (e.g. online) will be defined during implementation of the grant and may make use of existing platforms).

1.3.6 Location and description of samples in existing biorepositories.

- Collect information on the location of biorepositories and associated metadata, including bacterial species, susceptibility status, and the existence of associated epidemiological data.
- Describe the storage conditions and likely viability of samples.
- Provide the information to the Management Agent on location and types of bio-repositories alongside recommendations for the use of the isolates. Recommendations may include use of genomic analysis and use of these to improve quality assurance and control.

1.3.7 Conducting advocacy for improved data quality and submission of prospective date.

Make recommendations to sites which, if implemented, will facilitate ongoing sharing of data using a standard set of recommendations and advice on electronic record keeping and data sharing that aligns with GLASS and makes use of WHONET.

1.3.8 Report data at country level in a format useful for local policy makers

- Develop or consolidate situational analysis on data and the lack thereof on AMR and AMU in public health.
- Identify key areas and make specific suggestions for policy which would improve surveillance coverage and quality, treatment, the use of antibiotics and the use of data in evidenced based policy and practice.

1.4 Application requirement

1.4.1 Grant length and main deliverables

Regional Grants round 1 is planned for 18 months comprised of:

- An inception phase (3 months) to develop partnership in the region, develop a data quality grading system in collaboration with other regional grantees (through a workshop) to address the tasks of data collection analysis and reporting. The inception phase will also be used to develop management plans, risk-assessments, and workflow.
- Data collection in the region (12 months) and development of an analytical model in collaboration with other regional grantees to ensure alignment in common format, presentable, publishable among the four regions.
- Analysis and reporting (3 months): including a review workshop to examine collected data and launch the platform for data sharing.
- The expected start date will be no later than five months following submission of Expressions of Interest, and no later than four months following submission of Applications.

1.4.2 Grant eligibility criteria

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

- Must demonstrate they are competent organisations responding to this call for proposals and able to respond to each of the tasks outlined in this Terms of Reference.
- Have the appropriate track-record in clinical data collection, analysis and interpretation, including epidemiology, and operating in the designated regions.
- Can be a single organisation, a partnership or consortium, though the latter must clearly identify a Lead Grantee with the appropriate governance and coordination mechanisms to manage sub-grantees.
- Organisations can be:
    - Academic institutes – such as a university or research institutes.
    - Non-Governmental organisations.
    - Private companies.
    - Government-owned enterprises or institutions, provided they can establish that they are (i) legally and financially autonomous, (ii) operate under commercial law, and (iii) are not dependent agencies of national governments.
- Must demonstrate the ability to work in the assigned region.
- Should be able to provide all information required for grant-assurance 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.
- Where the application is from a consortium, the Lead Grantee must be able to provide the same information and assurances for all sub-grantees.

1.4.3 Application process

The application process will be undertaken in two stages.

Firstly, prospective grantees must register their interest by responding to a Request for EOI published on www.mottmac.com/fleming . The EOI will entail the completion of the Expression of Interest form describing:

- Which region(s) the applicant will operate in ‑ applicants may select one, more than one or all four regions.
- The approach to collect past and present AMR and AMU data.
- How the grantee will develop partnerships in the region.
- Present suggestions for a data quality grading system and analytical plans.
- Key personnel and their roles, proposed workplan, and a management structure.

Secondly, those organisations that are successfully reviewed at the EOI stage will then be asked to develop a full proposal and submit a Regional Grants application.

1.4.4 Evaluation criteria

The selection of the grantees to go to full proposal stage will be based on the concept note, track record and grant eligibility criteria.

1.4.5 Restrictions/limitations

Any conflict of interest, or potential conflict of interest, should be declared to Management Agent when prospective grantees are registering their interest to apply for a Regional 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 document.

1.4.6 Key dates

Publication of Request for EOI: 5 March 2018

EOI submission deadline: 26 March 2018 at 12:00 (GMT)

Request for Proposals: 16 April 2018

Full proposal submission deadline: 31 May 2018