



Antimicrobial Resistance (AMR) in the Real World – Announcement of Opportunity (AO) Research Grant Outlines

Closing date: 16:00 6 October 2015

Summary

Antimicrobial Resistance (AMR) in the Real World is a £6.5m programme under the AMR Cross-Council Initiative. This call is co-funded by the Natural Environment Research Council (NERC), the Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council (MRC), and has potential co-funding from the Arts and Humanities Research Council (AHRC).

The programme will support two types of award; larger Research Grants and smaller, more focused, Pump Priming Grants. This Announcement of Opportunity (AO) is for an outline stage for Research Grants which can be up to £1.5m (100% FEC) per project and up to four years' duration. The call for Pump Priming Grants will follow in due course.

This programme aims to address the need for a greater understanding of the role of the outdoor environment and host microbiome in influencing the evolution, acquisition and spread of antibacterial resistance, and acting as a reservoir for resistance. The programme is restricted to antibacterials and resistant bacteria or bacterial resistance genes, of clinical and/or veterinary importance. Research supported can be based in agricultural, aquaculture, wastewater and natural environments (and their interfaces), the human and animal host microbiome, and also includes elements of the way people and human communities interact with the environment. Proposals will need to be interdisciplinary and consider appropriate partnerships to meet the requirements of this call. We now invite outline applications to this call.

A town meeting, where applicants can gain additional information and discuss their potential proposals with the funders and potential collaborators and end users will be held in London on 11 September 2015.

1. Background

1.1 Strategic background

AMR is recognised as one of the most important global issues for human and animal health. There are increasing numbers of resistant infections, many existing antimicrobials are becoming less effective, and there is rapid spread of multi-drug resistance. This means that we could be close to a reality where we are unable to prevent or treat everyday infections/diseases. Furthermore, there is a lack of significant commercial innovation in antimicrobials. Part of the research challenge must

therefore be to conserve the antimicrobials we have left by understanding and mitigating the development of resistance. To develop a complete picture we need to understand the role of the outdoor and host environments in the development and transmission of AMR, an area where there has been very little co-ordinated research effort to date.

The UK Government has published a Five Year Antimicrobial Resistance Strategy¹ (2013-2018) that sets out the actions and research needed to tackle AMR. Both the Government's AMR Strategy and the Science & Technology Select Committee's recent report on Ensuring Access to Working Antimicrobials², have highlighted the need to understand AMR in the real world, and the Select Committee's report recommends "a research programme that will recruit expertise across the UK to fill the knowledge gaps on how antimicrobial resistance exists and may be transmitted via environmental routes".

1.2 Call background

The AMR Funders' Forum (AMRFF)³ and the AMR Cross-Council Initiative⁴ have been created to enable the interdisciplinary research required to address the issue of AMR.

The AMR Cross-Council Initiative is led by MRC on behalf of the Research Councils and will be delivered via a thematic approach with research to be commissioned under four themes:

- Theme 1: Understanding resistant bacteria in context of the host;
- Theme 2: Accelerating therapeutic and diagnostics development;
- Theme 3: Understanding the real world interactions;
- Theme 4: Behaviour within and beyond the health care setting.

A phased approach to delivery is being taken with the timing of calls under each of the themes being determined on a case-by-case basis. To date, the AMR Initiative has committed £28.5m to new research activities and the total investment will increase as new activities are commissioned.

This call, AMR in the Real World, falls under Theme 3 (Understanding the real world interactions) of the AMR Cross-Council Initiative. Theme 3 aims to address the need for a greater understanding of the role of the bacterial environment, defined in the broad sense (including host microbiomes), in influencing the evolution, acquisition and spread of antibacterial resistance, and as a reservoir of resistance. This programme is focused on AMR in outdoor environments and the host microbiome, but the Research Councils also recognise the importance of understanding AMR in indoor environments, such as hospitals and homes, and the Arts and Humanities Research Council (AHRC) are coordinating a scoping exercise to determine the research priorities in this area.

NERC are leading this programme on AMR in the Real World on behalf of the Research Councils. The research priorities for the programme were defined by two workshops in 2014 on AMR in the environment (specifically the outdoor environment) and AMR in the context of the host microbiome (both human and animal). These areas are being brought together to build the interdisciplinary science which is required to address the issues. This is a £6.5m programme co-funded by NERC (£3.5m), BBSRC (£2m) and MRC (£1m). In addition, AHRC will contribute on a case-by-case basis to successful projects with an arts and humanities component.

¹ <https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018>

² <http://www.publications.parliament.uk/pa/cm201415/cmselect/cmsctech/509/50902.htm>

³ <http://www.mrc.ac.uk/research/initiatives/antimicrobial-resistance/antimicrobial-resistance-funders-forum/>

⁴ <http://www.mrc.ac.uk/research/initiatives/antimicrobial-resistance/tackling-amr-a-cross-council-initiative/>

2. Grant requirements

Research Grants should be up to £1.5m (100% FEC), for up to four years' duration, intending to start no later than 1 May 2016 and complete by 31 March 2020.

2.1 Scope

This programme aims to address the need for a greater understanding of the role of the outdoor and host microbiome in influencing the evolution, acquisition and spread of antimicrobial resistance, and as a reservoir for resistance.

This programme is restricted to antibacterials and resistant bacteria or bacterial resistance genes, of clinical and/or veterinary importance, and excludes antibacterial resistance in plant pathogens.

Research supported can be based in agricultural, aquaculture, wastewater and natural environments (freshwater, marine, soil, air, etc. and their interfaces), human and animal host microbiomes (including the gut, skin, respiratory and oral microbiomes) and also includes elements relating to the way people and human communities interact with the environment, animals and each other. Research based in the indoor environment (e.g. looking at surfaces in hospitals) is outside of the scope of this programme.

As it will not be possible to cover the full scope of the programme within a single project it is expected that supported projects will focus their research questions around specific locations, specific antibacterials and/or specific bacterial communities, however applicants should set-out how the approaches and methodologies developed could be translated to other environments, antibacterials or other bacterial communities.

Proposals that include research within the remit of more than one of the Funders are welcome. AHRC will consider funding on a case-by-case basis proposals with an arts and humanities component. Areas of interest to AHRC are briefly outlined within the work packages below but further detail of approaches and possible research questions are detailed in Annex 1. As the environmental science elements of this call are predominately in Work Package 1, it is expected that at least £3m of the NERC contribution to the call (£3.5m) will be invested in this work package.

A key aim of this programme is to develop a community of researchers with the broad range of skills and expertise needed to understand the evolution, acquisition and spread of antimicrobial resistance. This will include learning from and building on research in related areas, and applications from researchers who have not worked on AMR previously but have experience in relevant disciplines, such as environmental microbiology, gut microbiology, bacteriology or arts and humanities, are encouraged as the Funders are keen to expand the AMR research base in the UK.

2.2 Scientific objectives

There are two work packages as part of this programme. Proposals can address either Work Package 1 or Work Package 2, or can work across both work packages. In all cases applicants must clearly demonstrate how their project will deliver against the objectives of the relevant work package(s).

Work package 1

Within this work package, we specifically want to advance understanding of the acquisition, spread and evolution of AMR in the environment and to determine how this affects exposure risks for humans/animals.

Applicants must address one or more of the following three issues:

1. Understanding sources, presence, location, transport, fluxes, transformations and eventual fate of antibacterials in the environment, at an appropriate spatial and temporal scale, and relating this to usage and professional practices.
2. Understanding presence, location and levels of resistant bacteria and/or resistance genes in the environment (including measures of abundance, not just presence/absence) and how these genes are transferred within and between microbial communities (including non-pathogenic bacterial communities) and the rate at which they do so. Applicants should identify the implications for pathogens of clinical and/or veterinary importance.
3. Developing a quantitative understanding of the processes and factors that control the selection of AMR genes in the environment, including:
 - emergence of resistance (including via novel mechanisms);
 - persistence/retention (including both survival and fitness effects);
 - transfer;
 - evolution; and
 - co-selection.

This work should identify the specific environmental drivers of these selection processes, including both anthropogenic and non-anthropogenic drivers. The work should also include identifying the implications for pathogens of clinical and/or veterinary importance.

Within the projects applicants should also begin exploring how their research can inform AMR policy and management strategies. The range of research of relevance to policy is broad and some examples are listed below, note that this list is not exhaustive and research in other areas that can contribute to policy development is also welcome:

- Predict the exposure risk to humans/animals (including identifying hotspot locations for exposure and locations susceptible to emergence of resistance) and the corresponding implications for health. How the presence of humans/animals plays a part in the acquisition, spread and evolution of AMR in the environment could also be considered.
- Explore potential interventions and mitigation strategies, including new strategies, which minimise the emergence, transmission, and/or exposure risk of resistance in the environment in a cost-effective, sustainable way. Potential interventions could include physical solutions to prevent the spread of antibacterial resistance and suggested changes in environmental, agricultural, veterinary and medical management practices. Proposals that consider cultural factors around different practices (including professional practices) and community contexts, for example exploring participatory approaches to co-design interventions with diverse communities or using visualisation, narrative and/or creative arts approaches to engage diverse communities, are eligible to apply. Identifying or developing new antimicrobials or the design and use of indoor environments is outside the scope.

Work package 2

Within this work package, we specifically want to advance understanding of the acquisition, spread and evolution of AMR in the host microbiome (human and animal), and the potential role of the environment in this.

Research proposals should aim to develop an understanding of AMR genes and resistant bacteria in the context of host microbiomes, through one or more of the following:

- interactions between resistant bacteria and the wider microbial community in the host (including gut, skin, oral, respiratory, etc.);
- specific drivers of the emergence, evolution and co-selection of resistance;
- persistence/retention (including both survival and fitness effects);
- how resistance genes are transferred within the microbiome, including pathogenic and commensal bacteria;
- the influence of the 'outdoor' environment on these and the interaction between the host and the environment.

Applicants should identify whether the presence of resistant bacteria or resistance genes in the host microbiome has implications for pathogens of clinical and/or veterinary importance.

2.3 Non-scientific objectives

Proposals will address the following objectives:

1. Interdisciplinary collaborations

Applicants must consider appropriate collaborative partnerships between disciplines to tackle this research such as: bacteriology, veterinary science, ecology, informatics and computational modelling, mathematics and the arts and humanities. Attracting new disciplines to the field of AMR research is a key goal for the over-arching cross-Council initiative.

2. Partnerships

The funders strongly encourage projects to engage with potential partnerships to ensure that the research proposals are designed to provide the evidence needed to support policy/regulators and/or industry, as appropriate. There should also be a consideration of the antibacterial prescribers and users, including farmers, veterinary and medical practitioners, and the public. Appropriate involvement of such partners should be part of the project design in order to ensure appropriate pathways to impact.

Where possible applicants should include partnership activities with new or existing partners and align with on-going activities to develop new ways of working. Some organisations who have indicated in advance a desire to partner with applicants to this call can be found in Annex 2. **There is no obligation to include any of the partners listed in Annex 2 and the inclusion of partners in organisations not included in Annex 2 is also encouraged. Co-funding from industry/policy partners is not a prerequisite for this call.** However, it is a requirement that the research is of relevance to users and that projects have appropriate user engagement mechanisms in place, and applicants should ensure these issues are addressed in the proposals.

2.4 Eligibility

All applicants must meet the organisation eligibility requirements of at least one of the funding organisations (AHRC, BBSRC, MRC or NERC), see <http://www.rcuk.ac.uk/funding/eligibilityforrcs/> for details of eligibility requirements of each of the councils. Eligibility criteria for investigators is given in the NERC grants handbook⁵.

Investigators may be named on a maximum of two different Research Grant proposals but only one as the lead Principal Investigator. It is the responsibility of the lead PI to ensure that your proposal does not include ineligible Co-Is and Researcher Co-Is, or any applicants who are named on more than two proposals. Proposals which break this eligibility rule will be rejected. Applications to the Research Grant call will be counted separately to the Pump Priming Grants call.

Centre for Environment, Fisheries and Aquaculture Science (Cefas)

In addition to the £6.5m of Research Councils' funding for this call, Cefas has made up to £200k available to cover their researchers' costs on proposals. Applicants from Cefas can be named on a proposal as Co-Investigators as long as there is a Principal Investigator from a Research Council eligible institution.

If you are requesting funding from Cefas you must:

1. Have agreement from Cefas that the project will be supported (see contact below) with an email or letter uploaded as an attachment on the Je-S system.
2. Clearly delineate the planned Cefas researchers' role in the project in the Case for Support.
3. Clearly outline the Cefas researchers' costs in the Justification of Resources and clearly indicate the funds requested from the Research councils on the Je-S system. ONLY Research Council funds should be requested through Je-S. Non-eligible Co-Is should be listed with no associated costs. Proposals where the costing is unclear will be rejected.

Due to these additional eligibility options, it is expected that proposals DO NOT include Cefas as sub-contractors on proposals. Proposals which list Cefas as a sub-contractor will not be accepted. However, any project requiring the use of Cefas facilities where there is a Cefas CoI, should request the facilities costs and associated consumables but applicants should ensure that any use of Cefas facilities, as with all costs, are fully justified in the Justification of Resources.

Cefas funding queries: Lisa Sivyer (Lisa.sivyer@cefas.co.uk).

Normal RCUK eligibility rules apply to other government funded research institutions.

2.5 Studentships

No associated studentships are permitted.

3. Process and assessment

3.1 Overview of programme delivery

This is one of two parts of the programme AMR in the Real World. This AO is for Outline larger Research Grants. These will be assessed by an expert panel and successful Outlines will be invited to

⁵ <http://www.nerc.ac.uk/funding/application/howtoapply/forms/grantshandbook/>

submit Full Proposals. Full larger Research Grant Proposals will be sent out for international peer review and Principal Investigators will be given the opportunity to respond to reviewer comments ahead of the panel meeting.

The AO for the smaller Pump Priming Grants will be published in August 2015. These smaller Pump Priming Grants will be around £200k (100% FEC) for 12-36 months to stimulate “high risk/high reward” projects and new innovations. These Pump Priming Grants will have the same science scope as the Research Grants, but proposals will be expected to have a narrower focus than the larger Research Grants, and so may address only part of one of the three main issues identified under each work package. The Pump Priming Grants call will have the same closing date as the larger Research Grants Full Proposals and will be considered by the same panel.

The panel will look across the grants and assess the potential for the projects to deliver a balanced portfolio which address the programme objectives. The funders reserve the right not to fund up to the limit allocated to the programme, and will consider the overall balance of science needed to deliver the programme, in making decisions about which grants to fund.

3.2 Programme coordination and integration

Following the award of grants, additional funds will be available to deliver activities designed to improve integration and coordination of research efforts (such as synthesis activities and science meetings) but also carry out Knowledge Exchange, impact and innovation activities. This will be across the projects in this programme but also link with the other themes of the AMR Cross-Council Initiative where appropriate. This activity will specifically facilitate interdisciplinary and whole system working.

3.3 Town Meeting

Given the complexity of the research challenges addressed by this call, and the need to develop new partnerships and collaborations, the funders will be holding a Town Meeting on 11 September 2015. This will provide the opportunity to hear more from the funders of this call, network across the various disciplines, identify potential collaborators and stakeholders, and to discuss areas for potential applications. Individuals interested in either the Research Grants or the Pump Priming Grants are actively encouraged to take part in the Town Meeting, but participation in this meeting is not a requirement of call.

3.4 Application process for this call

3.4.1 Outline stage

One Outline is required for each proposed Research Grant project; i.e. projects that expect to be submitted as joint proposals at the Full Proposal stage need only submit one Outline covering the whole project. It is expected that the Outline will be submitted by the Principal Investigator.

For all Outlines, the PI must submit a completed Outline proforma, which can be downloaded from the NERC website at <http://www.nerc.ac.uk/research/funded/programmes/amr/news/ao-outline/amr-ao-form>. Completed Outlines must be submitted to the email address: amr@nerc.ac.uk by 16:00 BST on 6 October 2015. Outlines received after this date and time will not be accepted.

Any Outline which does not use the template provided, comply with these specifications or exceeds the stated word limits will be rejected prior to the panel. Outlines should be submitted in word format. No additional attachments will be accepted.

Applicants should consider the fit to the scope, scientific objectives and non-scientific objectives when completing their proforma.

Applicants are not expected to include a detailed breakdown of costs at this stage, but are asked to provide an estimate of the total funding that will be requested from the Research Councils. Details of eligible costs can be found in the NERC grants handbook⁶.

3.4.2 Full Proposal stage

Only applicants successful at the Outline stage will be invited to proceed to the Full Proposal stage. It is expected that proposals will evolve between the Outline and the Full Proposal (including personnel), but major science elements of the project proposed are expected to remain broadly the same, within the confines of any feedback from the Outline stage. Applicants should agree any significant proposed changes with the Research Councils prior to submitting their Full Proposals; all requests to modify the scope of projects should be sent to amr@nerc.ac.uk who will coordinate the Councils' response to requests.

Details on the submission and assessment procedures for Full Proposals will be provided to the PIs of successful Outlines. As an indication of expectations for this stage, Full Proposals will be submitted through JeS, have a similar format to NERC Discovery Science Standard Grants, and the primary assessment criteria will be Excellence and Fit to Scheme. The deadline for Full Proposals will be 3 December 2015.

3.5 Assessment process

Outlines received prior to the deadline which fit the basic requirements of the call will be assessed by an Assessment Panel that will shortlist those that will be invited to submit Full Proposals.

Proposals will be assessed on remit, Fit to Scheme (scientific and non-scientific objectives) and *potential* for Excellence. The funders will consider the overall balance of science needed to deliver the programme in making decisions about which Outline proposals are progressed to the Full Proposal stage.

Applicants will be given brief feedback from the Panel summarising the reasons why the Outline was successful/unsuccessful. No further feedback will be available.

4. Timeline

AO for Research Grant Outlines launched	July 2015
Call for Town Meeting released	July 2015
AO for Pump Priming Grants launched	August 2015
Town Meeting	11 September 2015
Closing date for Research Grant Outlines	6 October 2015
Assessment panel for Research Grant Outlines	October 2015
Closing date for Full Proposal Research Grants and Pump Priming Grants	3 December 2015

⁶ <http://www.nerc.ac.uk/funding/application/howtoapply/forms/grantshandbook/>

Full Proposal Research Grants and Pump Priming Grants Panel
Research Grants and Pump Priming Grants start
All grants will have completed by

March 2016
1 May 2016
31 March 2020

6. Contacts

Scientific queries, application process and general enquiries:

Daniel Knight

amr@nerc.ac.uk

01793 411672

For queries on specific council remit please contact:

AHRC:

Gail Lambourne

G.Lambourne@ahrc.ac.uk

BBSRC:

Sian Rowland

amr@bbsrc.ac.uk

MRC:

Ghada Zoubiane

amr@headoffice.mrc.ac.uk

Cefas funding queries:

Lisa Sivyver

Lisa.sivyver@cefas.co.uk

Annex 1

Specifications of approaches and potential research questions of interest to AHRC

Proposals to this call with an arts and humanities component will be considered by AHRC on a case-by-case basis.

To fully understand the interaction between people, communities (including professional) and the environment and its role in AMR, the use of a wide range of approaches and methods could be utilised as part of arts and humanities research. This could include ethnography, creative expression, history, literature, design and the use of narrative and storytelling to understand the complexity of these interactions.

Research questions could include:

- Working with professional and local communities to develop more sustainable practices to help mitigate AMR development/emergence in the environment through for example:
 - o Improving understanding of changes in environmental, landscape and agricultural management practices, and public health over time and applying this to modern contexts;
 - o learning from past successes and failures in engaging communities (including professional communities) in this area;
 - o employing participatory approaches to co-design interventions with diverse communities;
 - o using visualisation, narrative and/or creative arts approaches to engage diverse communities in mitigation strategies focused around the interface and relationship between AMR and the environment;
 - o understanding the impact of cultural factors (historical perspectives, beliefs, cultural values, ethnicity) and cultural inequalities in developing (multi-level) intervention and mitigation strategies;
- What approaches are most effective in different groups?
- How sensitive is AMR emergence to community contexts, including the practices of professional communities?
- How can services be integrated in such a way to take into account the above factors to transform health practices and processes of user engagement?
- Understanding the take-up/scaling-up of interventions which work and how better understanding of cultural and professional practices and traditions can help more effective scaling up of interventions.

Annex 2

Potential project partners which applicants may wish to approach

Several organisations have expressed an interest in contributing resources to individual projects for this call. Applicants can approach any of these of relevance but are not obliged to include any of these organisations.

Industry

Agriculture and Horticulture Development Board (AHDB)

Where proposals are interested in systems of relevance to the pork, beef, lamb or dairy sectors, applicants may wish to approach AHDB for which they can provide access to strategic work of relevance, EU collaborative research groups and Knowledge Transfer avenues within the organisation. Please contact Martin Smith (Martin.Smith@ahdb.org.uk).

AstraZeneca

Where proposals seek to provide novel tools and approaches that could (i) underpin the prospective environmental risk assessment of antibacterials and associated antibacterial resistance and (ii) target retrospective environmental risk management and mitigation strategies for resistance that encompass the pressures of co-selection and fitness etc. applicants may wish to approach AstraZeneca as a project partner for which they could provide advice, data, other forms of in kind support and in-part funding, as appropriate. Please contact Jason Snape (Jason.Snape@astrazeneca.com).

Scottish Salmon Producers' Organisation

Where proposals have any relevance to Scottish salmon aquaculture, applicants may wish to approach SSPO as a project partner for which they could provide knowledge, access to information and resources. Please contact Dr John L Webster, Technical Director (JWebster@scottishsalmon.co.uk).

Water Industry Research Group

Where proposals cover aspects of wastewater discharges, applicants may wish to approach UK Water Industry Research ("UKWIR") to identify a possible project partner from the UK sewerage companies. Such partners may be able to offer access to sites, advice, data, and other forms of in kind support, as appropriate. Hans Jensen is Chief Executive of UKWIR, and the programme lead for wastewater is Howard Brett (howard.brett@thameswater.co.uk).

Government departments and agencies

Environment Agency

The Environment Agency regulate intensive farming, the spreading of material to land (e.g. sewage sludge, digestate, animal by-product treated material) and the discharge of treated wastewater to water bodies. Where proposals seek to further our understanding of the emergence, dissemination and impact upon environmental quality and health of antimicrobials, antibiotic residues, antimicrobial resistant bacteria and genes from such activities, applicants may approach the Environment Agency as a project partner. In addition to being an end-user of the information, they could facilitate access to pig and poultry sites, provide technical expertise, access to data and other forms of in kind support, as appropriate. Please contact Alwyn Hart (alwyn.hart@environment-agency.gov.uk).

Food Standards Agency (FSA)

The FSA is commissioning a systematic review on the contribution that food makes to AMR which it hopes will report in early 2016. The FSA would be interested to hear from applicants to this call who may be considering proposals which have the potential to address key evidence gaps in this area. Please contact Alisdair Wotherspoon in the first instance (Alisdair.wotherspoon@foodstandards.gsi.gov.uk).

Natural England

Of England's 224 National Nature Reserves (NNRs), Natural England are responsible for the management of 143 sites directly, 23 of which are managed in partnership or in various forms of shared management with Approved Bodies. Almost the entire NNR area is SSSI (over 99% by area) and 84% of NNRs are also either SAC or SPA (or both). Natural England are offering their 143 NNRs as potential sample sights as part of this call. This would provide researchers with a range of environments from the relatively wild uplands of northern Pennines to coastal sites. Some sites are actively managed with stock, whilst others are not. For more information please contact Dave Stone, Dave.Stone@naturalengland.org.uk.