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House of Commons
Science and Technology
Committee

**Ensuring access to
working
antimicrobials:
Research Councils UK
Response to the
Committee's First
Report of
Session 2014–15**

**Third Special Report of
Session 2014–15**

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Third Special Report

On 7 July 2014 the Science and Technology Committee published its First Report of Session 2014–15, *Ensuring access to working antimicrobials* [HC 509]. On 20 August 2014 the Committee received a memorandum from the Research Councils UK which contained a response to the Report. The memorandum is published as Appendix 1 to the Report.

Appendix 1: Research Councils UK response

Research Councils UK is pleased to be able to respond to the above report on behalf of all of the seven research councils. This response has been shared and discussed with the Department of Health to complement the Government response by expanding on the research issues raised within the report.

The research councils strongly endorse the Committee's recommendations and strong emphasis on research-based practice. This response will, firstly, highlight the significant research activity across the councils and, secondly, specifically respond to some of the recommendations made by the Committee.

Cross-council research activity

The Antimicrobial Resistance Funders Forum¹

The UK research base in antimicrobial resistance (AMR) is supported by a range of funders, including public sector organisations, charities and industry. However, as highlighted in the report, a single body needs to "take action and corral the efforts". To this end, the Antimicrobial Resistance Funders' Forum (AMRFF) has been established to provide a forum for the sharing of information on activities relating to AMR by the various member organisations, with a particular focus on anti-bacterial resistance in humans and farm animals. The AMRFF provides a framework for a more coordinated approach to tackling AMR research to maximise impact on national and international policies and activities.

Specifically, the key aims of the AMRFF are to:

- Take a strategic view of the UK AMR research base with an understanding of its output, skill base, resources and impact
- Create a common vision for the future of AMR research and its implementation

¹ www.mrc.ac.uk/amr

- Add value to existing programmes of work through coordination, synergy of activities and gap awareness
- Coordinate and/or support the initiation of unilateral, bilateral or multilateral funding and delivery programmes
- Raise the understanding and profile of AMR research base in the UK and internationally through proactive communication with all stakeholders

The AMRFF is led by the MRC and membership includes all of the research councils, UK Health Departments, governmental bodies, as well as charities that have a direct or indirect interest in AMR and provide significant R&D budgets in the area.

- Arts and Humanities Research Council (AHRC)
- Biotechnology and Biological Sciences Research Council (BBSRC)
- Department of Business, Innovation and Skills (BIS)
- Defence Science and Technology Laboratory (Dstl)
- Department for the environment, food & rural affairs (Defra) & Veterinary Medicines Directorate (VMD)
- Department for International Development (DFID)
- Department of Health (DH)
- Economic and Social Research Council (ESRC)
- Engineering and Physical Sciences Research Council (EPSRC)
- The Food Standards Agency (FSA)
- HSC R&D Division, Public Health Agency, Northern Ireland
- Medical Research Council (MRC)
- Natural Environment Research Council (NERC)
- National Institute of Health Research (NIHR)
- Science and Technology Facilities Research Council (STFC)
- Technology Strategy Board (TSB)
- Wellcome Trust

Forum members held a number of workshops and discussions throughout 2013 and 2014 to identify the research challenges and opportunities as well as needs. There was a very strong call for research to be multidisciplinary, calling on the expertise of a broader range of expertise than may currently be involved—for example, bacteriologists working alongside clinicians, veterinarians, engineers, chemists, environmental scientists,

geneticists, social scientists and more. It was also considered essential that research is relevant to humans and animals under a "one health" agenda.

The research councils have also developed strong international links in AMR. The MRC leads, on behalf of the UK, on a Joint Programming Initiative (JPI) with EU member states—"The microbial challenge—an emerging threat to human health". We have developed and launched a Strategic Research Agenda (SRA) as well as call to fund research proposals. We have established two research consortia in partnership with the Canadian Institute of Health Research (CIHR). The MRC is the BIS appointed UK representative on the State Representative Group for the EU and European Federation of Pharmaceutical Industries and Associations (EFPIA) "Innovative Medicines Initiative (IMI)". To date €431m has been committed to five AMR consortia across Europe with UK researchers involved in a number of these. BBSRC is contributing to the Animal Health and Welfare ERA-Net, an EU wide funding programme as well as an international Veterinary Vaccinology Research Network. The research councils are currently developing links with China, India and Brazil in the AMR area to answer research questions globally.

Addressing the challenges – a thematic approach

Through the work of the AMRFF, four key themes have emerged that require a multidisciplinary approach and are considered essential to tackling AMR.

Theme 1: Understanding resistant bacteria in context of the host

Despite a strong basic bacteriology portfolio across the UK, funded through a number of sources, there are still many gaps in our understanding of the molecular and cellular biology of bacterial resistance, especially how bacteria evolve, acquire and transmit antibiotic resistance and how they adapt to life in human and animal hosts. This theme will aim to take a multidisciplinary approach to understand how resistance develops and is transmitted.

Theme 2: Accelerating therapeutic and diagnostics development

This theme will cover the discovery of new antibiotics as well as revisit old antibiotics with new scientific approaches to enhance their usefulness. It will also look to developing new, non-traditional antibiotic treatments. The science will build on discoveries made as part of theme 1 as well as on existing research programmes. This theme also emphasises the importance of developing new technologies for identifying resistant bacteria, to underpin diagnostics development and so better target any new therapies. Finally, the research in this theme may provide a real-life test bed studying the impact of different economic and business models, or development of novel business models, related to the process and drivers of innovation in the development of new antibiotics and diagnostics.

Theme 3: Understanding the real world interactions

It is clear that the environment, and the way people and communities interact with the environment, hugely influences the way bacteria behave and the transmission of genes within and between bacterial species. A greater understanding of how differing environments and their uses influence the evolution, acquisition and spread of antibiotic resistance and reservoirs of resistance is therefore needed. Here the “environment” is seen in its broadest sense from host tissues to man-made settings and natural environments. This would encompass, for example, human and animal intestinal tracts, wounds in humans and animals, hospitals, care homes and transport systems, all the way through to waste water, agricultural and natural environments (freshwater, marine, soil, air, etc. and their interfaces). Understanding these environments and their role in resistance will help identify and target better prevention measures and management practices.

Theme 4: Behaviour within and beyond the health care setting

This theme will aim to elucidate the underpinning motivations for human behaviours relating to AMR, and how behaviour can affect development and spread of antibacterial resistance. It will also explore how to best enable effective behaviour change interventions in a variety of settings, relevant to both humans and animals. It may also serve as the basis for research into the economics of AMR.

The research councils are now launching initiatives, ring fencing funds from current headroom, to address these themes. MRC and BBSRC are investing £20m in themes 1 and 2 and calls have now been launched. EPSRC, recognising the important role that engineering and physical sciences can play in this challenge, are investing £5m to encourage universities to build capacity and understanding through multidisciplinary networks focussed on the four key themes identified. Themes 3 and 4 are in development and NERC and ESRC are playing a key role in shaping future calls in consultation with other potential partners, including BBSRC, MRC, EPSRC and AHRC. All funding will be reviewed for scientific excellence by expert panels, consisting of both international leading academics and relevant industry. The initiative will be overseen by a specialist steering group of national, international and private sector experts.

Response to specific report recommendations:

5. Diagnostics are a key tool in limiting and targeting use of antibiotics. The Government should indicate in its response to this report how it intends to ensure better use of current diagnostic facilities, how it intends to speed up diagnostic provision and how it will ensure that the Catapult for Precision Medicine delivers diagnostics for infectious diseases.

In recognition of the importance of diagnostics, theme 2 of the AMRFF initiative specifically calls for research proposals to develop new diagnostics. This will build on the expertise of the academic sector but is also expected to link strongly with the private sector.

The research councils have developed strong working relationships with TSB and their position on the AMRFF will ensure alignment of their activity with the research councils. The research councils have worked closely with TSB on the development of the Precision Medicine Catapult to accelerate diagnostics development. The research councils also look forward to working with NESTA on the Longitude Prize which will be focussed on new diagnostic tools for antibiotics.

The report already recognises the cutting edge work of the EPSRC interdisciplinary research collaboration, i-Sense, in UCL to create a new generation of early-warning sensing systems for diagnosis, monitoring and prevention of the spread of infectious diseases. Elsewhere, the MRC has worked in partnership with TSB, BBSRC and Defra to fund research on the detection and identification of infectious agents.

One other important aspect is the detection of genes which confer anti-microbial resistance. Advances in next-generation sequencing at BBSRC, MRC and NERC centres will allow for more rapid identification of resistance genes and the ability to attribute these genes to a potential source.

9. *"The Government recognises that there is a lack of information concerning environmental drivers of antimicrobial resistance. We recommend that the Government publish, in its Action Plan, 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. Hoping that research grant applications to research councils will serendipitously gather this necessary information leaves too much to chance. Research council funding should be, in this important field of study, complementary to Government directed, and funded, research programmes."*

The research councils fully endorse the necessity of understanding the impact of the environment on antimicrobial resistance and have funded work through response mode mechanisms. For example, NERC have funded a study "Finding hidden AMR in the environment" at the University of Warwick that examines the link between the environment, bacteria and human health by looking at the impact of sewage treatment on AMR bacteria in a river. Another example is a BBSRC-funded study at the University of Exeter to determine whether the low levels of antibiotics in the environment, from both humans and animals, could be contributing to AMR.

We agree too that there should be better coordination of research and more investment into environmental factors. To highlight this, the AMRFF has identified this as one of their key themes for future research. The role of the environment in AMR will be comprehensively addressed through multidisciplinary research plans being developed by the research councils to "Understand the real world interactions". There is an expectation that funding will be ring fenced from current headroom to fund environmental science in areas that have also been highlighted by the Committee.

10: *"There is circumstantial evidence that antimicrobial resistance can be transmitted from animal pathogens to human pathogens although the evidence base is incomplete. The Government needs to ensure that this is addressed. We recommend that this is an additional focus of research in the action plan and that in the meantime, the*

Government takes action to ensure the use of antibiotics in farm animals is strictly required for therapeutic use."

The research councils and AMRFF agree that this is an important area to study. The research themes developed all fall under the "One Health" umbrella and collaboration between human and animal researchers will be essential. The BBSRC brings strong expertise in basic animal bacteriology and veterinary medicine, and there will be close alignment with Defra and Veterinary Medicines Agency through the AMRFF. Research into animal pathogens will be included in the first two themes of the cross council initiative highlighted above.

12: "As the development of new antibiotics and new technologies is dependent on private enterprise working closely with academia, we were disappointed to find that the membership of the Government's High Level Steering Group for the Strategy did not incorporate voices from industry or learned societies. We recommend that the membership of the High Level Steering Group be expanded to include those voices."

The research councils are actively encouraging engagement with private sector partners and the involvement of the private sector will be essential at all stages of research and development. There is now a wealth of experience within the research councils in working with companies, from small one-to-one initiatives through to larger, multi-sector, multi-partner consortia and networks. The addition of the TSB to the AMRFF brings the ability to fund directly into smaller companies, which will allow us to develop public/private partnerships. The review mechanisms for funding research through our four themes above will include expertise from the private sector as will the top level governance group.

Many of the key learned societies (Biochemical Society, British Society for Antimicrobial Chemotherapy, Royal Society of Chemistry, Society for Applied Microbiology, Society for General Microbiology and Society of Biology) have formed their own AMR group and a number of AMRFF members attend these to ensure a joined-up approach. We will continue these discussions as we develop our plans. We will also continue our close engagement with senior academic colleagues across the disciplines and ensure through working closely with DH that communicate advice and opinion from academic, industrial and learned societies are communicated to the HLSG.

13 & 14: "Antimicrobial resistance has the potential to send medicine back to the early 20th century, severely limiting the use of what are now considered basic and routine surgical procedures. The best current defence against this scenario is a strong global pipeline of new drugs, possibly using a range of solutions as described above. But that is dependent on the infrastructure that provides financial incentive to the industries that deliver these technologies including means of compensating for the uncertainties inherent in research and development."

We agree with the Prime Minister that, if there is no change to the economic landscape for developing new antimicrobials, the pipeline of new antimicrobials will run dry. We also agree that the Government needs to work with researchers, investors, small and medium sized enterprises, large pharmaceutical companies and other Governments to urgently identify appropriate economic models that might encourage the development

of new antimicrobials. We hope that the review, which will take almost two years to report back with recommendations, will not delay work on any pricing alternatives that could be agreed with the pharmaceutical industry over a shorter timescale.”

The research councils fully support the work being done on economic models to encourage development of new antibiotics – it is essential to address these issues. The ESRC will work with the recently announced commission, and themes 2 and 4 of the research councils' initiative will also address some elements of the business and economic modelling.

The pull-through generated by these economic models is one essential part of the fight against AMR but the pipeline of new treatments also needs to be restocked. This will be driven by a range of factors such as better understanding of how resistance occurs and is spread, identification of new “druggable” targets in bacteria, better ways of screening new compounds, targeted delivery mechanisms, new treatment paradigms and beyond. The thematic approach taken by the research councils aims to tackle many of these questions. Theme 1—Understanding resistant bacteria in context of the host—will focus on deeper understanding of bacterial resistance with the aim of identifying new ways to beat antibiotic resistance. Theme 2—Accelerating therapeutic and diagnostics development—will address some of the important questions around developing these treatments, be they small molecule antibiotics or novel treatment regimes. As discussed above, this theme will also look at developing novel diagnostics to identify the infection and target the best treatment.

By utilising the latest chemistry and engineering, the advent of new synthetic biology techniques, advances in industrial biotech, coupled with the detailed understanding of bacterial cells, there has never been a better time to address the challenge of discovering new antibiotics. Building on the advanced knowledge in the research base, the research councils will work closely with TSB and the pharmaceutical industry to help improve the pipeline of new antibiotics.

Summary

The research councils welcome the Science & Technology Committee's report and the opportunity to highlight the action that is already or soon to be put in place to address some of the concerns. All seven of the research councils are investing in this area and we are co-ordinating our efforts with other funders through the AMRFF. We are strongly aligned with the Department of Health, Defra and devolved equivalents to ensure join-up of our research with other Government agencies and pull-through to policy and practice, while also engaging the private sector at the earliest opportunities for maximum buy in.



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