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UK Five Year Antimicrobial Resistance Strategy 2013 to 2018



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UK Five Year Antimicrobial Resistance Strategy

2013 to 2018

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Acknowledgements

This integrated 'UK Five Year Antimicrobial Resistance (AMR) Strategy', has been developed in collaboration with the Veterinary Medicines Directorate (VMD) of the Department for Environment, Food and Rural Affairs (Defra), the Northern Ireland Executive, the Scottish government, the Welsh government and the UK Public Health agencies. It reflects significant input from other government departments including the Department for Business Innovation and Skills (BIS) and the Ministry of Defence (MOD), as well as Government Agencies including the Food Standards Agency (FSA) and the Medicines and Healthcare products Regulatory Agency (MHRA). The National Health Service (NHS) including NHS England, experts from academia, the Research Councils, Go Science and several government advisory committees have also contributed to this work. In addition, views on the draft UK AMR Strategy and impact assessment were sought from independent bodies by means of a technical engagement exercise held in October 2012. A full list of organisations contributing to this work is provided in Annex A.

Foreword

There are few public health issues of greater importance than antimicrobial resistance (AMR) in terms of impact on society. This problem is not restricted to the UK. It concerns the entire world and requires action at local, national and global level. AMR cannot be eradicated but a multi-disciplinary approach involving a wide range of partners will limit the risk of AMR and minimise its impact for health, now and in the future.

The harsh reality is that infections are increasingly developing that cannot be treated. The rapid spread of multi-drug resistant (MDR) bacteria means that we could be close to reaching a point where we may not be able to prevent or treat everyday infections or diseases.

Many existing antimicrobials are becoming less effective. Bacteria, viruses and fungi are adapting naturally and becoming increasingly resistant to medicines used to treat the infections they cause. Inappropriate use of these valuable medicines has added to the problem.

Coupled to this, the development pipeline for new antibiotics is at an all-time low. We must therefore conserve the antibiotics we have left by using them optimally. The process of developing new antimicrobials and new technologies to allow quicker diagnosis and facilitate targeted treatment must be accelerated.

Information resources also need to be strengthened to support health professionals, their patients, animal keepers and the public, so that all understand the value and importance of antibiotics to society. This will only be achieved if human and veterinary health professionals work more closely with their patients and animal keepers, before deciding if an antibiotic is really needed and, in the event that it is, which one is most appropriate. This is in line with the aims of the global 'One-Health' approach¹ which spans people, animals, agriculture and the wider environment.

At the same time, we need even stronger international partnerships so that the threat of AMR is fully recognised and understood, with responsibility for reducing it shared. That is why we have been discussing with the World Health Organisation (WHO), the World Organisation for Animal Health (OIE) and others what more can be done to tackle the issue and achieve real progress in key areas within the next few years.

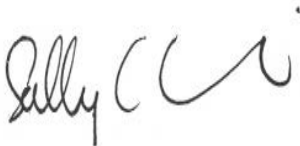
We need to get to a point where:

- good infection prevention and control measures to help prevent infections occurring become the norm in all sectors of human and animal health,
- infections can be diagnosed quickly and the right treatment used,
- patients and animal keepers fully understand the importance of antibiotic treatment regimens and adhere to them,
- surveillance is in place which quickly identifies new threats or changing patterns in resistance,
- there is a sustainable supply of new, effective antimicrobials.

This Strategy has been developed collaboratively with the UK devolved administrations and the bodies that will be responsible for delivering the work. It takes account of the 'Annual Report of

the Chief Medical Officer, 2011',² published in March 2013, which identified many of the priorities to be addressed and included a call to action.

Given the societal impact of this issue, it will be important that all sectors respond to the call for action set out in this Strategy if we are to successfully address this pressing problem and preserve our future healthcare.



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On behalf of the Chief Medical Officers and Chief Veterinary Officers in Northern Ireland, Scotland and Wales.

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1. Executive Summary

- 1.1 The scale of the threat of antimicrobial resistance (AMR) and the case for action was set out in the 'Annual Report of the Chief Medical Officer, 2011',² published in March 2013. This 'UK Five Year Antimicrobial Resistance Strategy 2013 to 2018' sets out actions to address the key challenges to AMR.
- 1.2 Modern medical practice relies on the widespread availability of effective antimicrobials to prevent and treat infections in humans and animals. Resistance to all antimicrobials, including antivirals and antifungals, is increasing, but of greatest concern is the rapid development of bacterial resistance to antibiotics. If the number of hard-to-treat infections continues to grow, then it will become increasingly difficult to control infection in a range of routine medical care settings and it will be more difficult to maintain animal health and protect animal welfare.
- 1.3 While we know that antibiotic resistance cannot be eradicated, it can be managed to limit the threat to, and minimise the impact on, human and animal health. This Strategy sets out how the UK intends to address the challenges detailed in the 'CMO's Annual Report'², as part of the 'One-Health' approach¹ which spans people, animals, agriculture and the wider environment. The Strategy has been informed by input from a wide range of experts in different disciplines and its delivery will involve many partners and require cross organisational co-operation at local, national and international levels.
- 1.4 The overarching goal of the Strategy is to slow the development and spread of AMR. It focusses activities around 3 strategic aims:
 - improve the knowledge and understanding of AMR,
 - conserve and steward the effectiveness of existing treatments,
 - stimulate the development of new antibiotics, diagnostics and novel therapies.
- 1.5 These aims will be underpinned by actions in 7 key areas, which have been informed by the '2011 EU AMR Strategic Action Plan',³ and address the 3 recommendations set out in the 'CMO's Annual Report'.² The Department of Health, with Department for Environment, Food and Rural Affairs (Defra) and Public Health England (PHE), will lead a wide-ranging programme of work involving organisations from public and private sectors in the UK and will continue to actively shape international activity.
- 1.6 Ensuring that antibiotics are used responsibly and less often will not happen overnight. It will require the full commitment and engagement of a range of experts, professionals and the public as part of a wider movement to change practices that have contributed to the rapid development of AMR and to reducing the effectiveness of many medical treatments. Everyone has a responsibility and a role to play in making this happen.

2. Introduction

- 2.1 Modern medical and veterinary practice relies on the widespread availability of effective antimicrobials to prevent and treat infections in humans and animals. Resistance to all antimicrobials, including antivirals and antifungals, is increasing. We recognise antimicrobial resistance is a broader issue than bacterial antibiotic resistance, but the scope of this Strategy is limited largely to the latter because of the rapid development of resistance to widely used antibiotics. Antibiotics have a variety of uses including treating and preventing infections and reducing the risk of potentially life threatening complications in surgery, chemotherapy and transplantation. Unless we act now we will see a rise in untreatable infections. Increasing scientific evidence suggests that the clinical issues with antimicrobial resistance that we face in human medicine are primarily the result of antibiotic use in people, rather than the use of antibiotics in animals. Nevertheless, use of antibiotics in animals (which includes fish, birds, bees and reptiles) is an important factor contributing to the wider pool of resistance which may have long term consequences.
- 2.2 Bacteria constantly evolve to maintain their viability in the face of the antibiotics used against them. Increasing resistance in Gram-negative bacteria, for example, *Escherichia coli* (*E. coli*) and *Klebsiella spp*, is a particular and growing public health concern because of the limited treatment options for infections caused by these bacteria, especially those that are resistant to carbapenem antibiotics, which are the last-line drugs used to treat those infections.
- 2.3 The initial emergence of resistance is random, arising by mutations (errors as DNA is copied in bacterial replication) or gene exchange among bacteria. The use of antibiotics then favours the spread of those bacteria that have become resistant. This is a complex issue driven by a variety of interconnected factors. Apart from the local weight of antibiotic usage, wider factors including increased travel and changes in population demographics also help resistant bacteria to spread. This makes an ever-changing disease burden more challenging to control both in the UK and globally. Given this dynamic picture there is a continuing need to support responsible antimicrobial use across all sectors to minimise antibiotic use and reduce the evolutionary pressures that encourage resistance.
- 2.4 The consequences of growing antimicrobial resistance extend beyond the human health sector. If the number of hard-to-treat infections continues to grow, not only will it become increasingly difficult to control infection in routine medical care, but it will be more difficult to maintain animal health and protect animal welfare. Treatment failure caused by AMR contributes to increased costs of care. The societal and economic costs of this are difficult to quantify, they include the health and economic burdens for the individual, their dependants, employers, businesses and the wider economy. In 2009, it was estimated by the European Centre for Disease Prevention and Control (ECDC) that AMR costs the EU about €1.5 billion in healthcare expenses and lost productivity each year.⁴
- 2.5 In 2012, the Department of Health commissioned the London School of Hygiene and Tropical Medicine and the University of Birmingham to investigate the economic burden of AMR.⁵ While the number of variables and uncertainties prevented

calculation of the full extent of the potential economic burden, it is clear from the economic analysis that resistance has the potential to have a major impact. There is much that is not known and more evidence will be required before the full extent of the economic and social burden of AMR can be determined.

An enduring problem

- 2.6 The importance of AMR has been recognised globally for many years. The first 'World Health Assembly (WHA) AMR resolution' was agreed in 1998 and urged Member States to take action to address AMR.⁶ The need to accelerate progress has been acknowledged by both the WHO and European Commission. The '2001 WHO Global Strategy for Containment of AMR',⁷ the '2011 EU AMR Strategic Action Plan',³ and the '2012 EU Council Conclusions'⁸ have all helped to provide a renewed focus on the area and informed development of this Strategy. In addition, work is being progressed to strengthen the legislative framework on the animal health side.
- 2.7 The first 'UK AMR Strategy, published in 2000',⁹ was developed in response to the recommendations contained in the Standing Medical Advisory Committee report 'Path of Least Resistance'¹⁰ produced in 1998. This led to significant changes including improvements in antibiotic use, increased funding for drug discovery programmes and extra support for research in the UK in the field of AMR. In parallel to this, new vaccine programmes as alternative approaches to infection management continue to be implemented, but AMR challenges remain.

Examples of actions taken in the UK to improve prescribing practice and other measures to tackle antibiotic resistance

Awareness raising activity

Since 2008, 'European Antibiotic Awareness Day' (EAAD) is held in November each year to raise awareness among health professionals and the public of AMR and appropriate prescribing. Evaluations of the activities have shown them to be cost-effective and successful in raising awareness of the issues and in driving behavioural changes. <http://ecdc.europa.eu/en/EAAD/Pages/Home.aspx/>

Optimising prescribing in Primary Care

We recognise that GP consultations can often be challenging, particularly when patients expect to receive antibiotics and may be unwilling to accept that they do not need them. To provide support for GPs in 2012, a GP toolkit – 'Treat Antibiotics Responsibly, Guidance and Education Tool' (TARGET) was developed by the then Health Protection Agency, in collaboration with several other professional bodies.[▲] It is hosted on the Royal College of General Practitioners website. www.RCGP.org.uk/TARGETantibiotics/

[▲] The 'Antimicrobial Stewardship in Primary Care' (ASIPC) Collaboration

There is another similar initiative, 'Stemming the Tide of Antibiotic Resistance' educational programme (STAR). This includes resources, for clinicians to share with the public during consultations, and is reported to have helped deliver changes in local prescribed practice and reduce unnecessary antibiotic use. Further details on the initiative are at: <http://www.stemmingthetide.org/>

Optimising prescribing in hospitals and antimicrobial stewardship

In recent years, hospital use of antibiotics has improved through the introduction of antimicrobial stewardship programmes involving a multi-professional specialist team in monitoring prescribing, resistance and infections, and supporting prescribers in choice and use of antibiotics. Resources like 'Start Smart then Focus' launched in 2011 have helped provide guidance on antibiotic stewardship in hospitals and encourage use of the right drug, right dose at the right time and right duration to limit unnecessary antibiotic exposure.

<https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus>

Prescribing measures

To improve prescribing, a number of measures relating to usage and choice of antibiotics were developed as part of the 'Quality, Innovation, Productivity and Prevention' (QIPP) programme in the NHS in England. They focused on reducing the overall use of antibiotics, reducing the use of cephalosporin and quinolone antibiotics (associated with an increased risk of *Clostridium difficile* infection), and recommending a 3 day course of trimethoprim for uncomplicated urinary tract infections, rather than longer courses. These measures are underpinned by authoritative, evidence based guidance developed by NICE. NHS organisations can access and compare prescribing rates through the 'NHS Prescription Services Portal'. <https://apps.nhsbsa.nhs.uk/infosystems/home/homepage.do>

Responsible prescribing in the veterinary sector

On the animal health side, concerted efforts across the veterinary and animal health sectors have led to a number of initiatives to promote the responsible use of antibiotics in animals. These include:

- the addition, by the Royal College of Veterinary Surgeons (RCVS), of a requirement within the 'Code of Professional Conduct for Veterinary Surgeons 2012'¹¹ for veterinarians to use antimicrobials responsibly to minimise development of resistance,
- formation of the Responsible Use of Medicines in Agriculture (RUMA) Alliance,¹² a cross industry alliance encompassing farming organisations, veterinarians, veterinary pharmaceutical industry, and retail organisations, which publishes responsible use guidance for each of the main food producing species,
- publication by the British Veterinary Association, the British Equine Veterinary Association and the British Small Animal Veterinary Association of general and species 'specific prescribing guidelines',

- production of 'leaflets on responsible use' by the Federation of Veterinarians of Europe (FVE) for vets and for the general public,
- A voluntary ban by the British Poultry Council on the use of certain antibiotics considered critically important for human health in day old chicks.

AMR Research

The UK Clinical Research Collaboration (UKCRC) 'Translational Infections Research Initiative' is a £16.5 million partnership of funders (DH / NIHR, MRC, Wellcome Trust and others) which runs from 2008 to 2015 to carry out research relevant to AMR and infection control. Outputs to date include: a systematic review of behaviour change strategies to influence antimicrobial prescribing in acute care and the promotion of mobile technology to change behaviour, educate and provide decision support to improve prescribing, for example, 'Imperial Antibiotic Prescribing Policy' (IAPP) which has won awards.

In October 2008 the Technology Strategy Board (TSB) was established by the Department for Business, Innovation and Skills (BIS) to provide an innovation platform to reduce the mortality, morbidity and economic burden of infectious disease in humans and animals. To date, £20 million has been invested to support the development of point of care diagnostics and to improve the ability of UK businesses to provide solutions for the global marketplace, boost UK economic performance and provide higher quality public services.

The 'Health Innovation Challenge Fund', a joint DH/ Wellcome Trust fund, is also providing £2.8 million over 3 years to research the use of genomic technology to inform outbreak recognition and national surveillance, which will help enable whole genome sequencing to improve patient care, local outbreak recognition and national surveillance.

Defra has funded 2 research projects at a cost of £1.1 million, completed in 2012 and 2013, into monitoring the incidence and spread of extended spectrum beta lactamase (ESBL) producing *E.coli* on farms. These bacteria provide enzymes that make them resistant to certain antibiotics.

Defra is also funding 4 additional research projects, on the use of antibiotics in food producing animals, at a cost of £2.2 million. One of these studies was completed in 2012, while the other 3 are due for completion in 2014, 2015 and 2016.

- 2.8 Despite these efforts, AMR has continued to escalate and further action is needed at a national and global level to make the level of progress at the pace needed to have a significant impact.
- 2.9 The second volume of the CMO's Annual Report,² published in March 2013, highlighted the need to act promptly and comprehensively to minimise the threats for human and animal health. The chapter on AMR identified the need to: preserve the effectiveness of our existing antimicrobial agents; encourage the development of new agents in the future; tackle poor domestic prescribing (which is fuelling resistance); and address the import of resistant bacteria from infections or colonisations acquired overseas, which pose an increased risk for security and resilience. It recognised that

the threat of AMR cannot be eradicated, but that it can be managed to minimise the impact for human and animal health. The report made 3 specific recommendations to address the AMR challenge and these are set out in the box below.

The CMO's AMR recommendations are:

1. Action is needed at the international, national and local level: antimicrobial resistance should be an issue that has the same level of political interest as methicillin resistant *Staphylococcus aureus* (MRSA) and *C. difficile* in England. It should be placed on the 'national risk register' (specifically, the "National Security Risk Assessment") and the government should campaign for it to be given higher priority internationally, including collaborations to ensure the development of new antimicrobials and vaccines such as Private Public Partnerships.
2. The national approach to tackling antimicrobial resistance should be managed jointly between DH and Defra to ensure that a comprehensive integrated programme is developed. The UK 2013 to 2018 cross government antimicrobial resistance strategy and action plan is welcome. It provides a base for future working but this needs to be built upon.
3. Rapid diagnostics enabling appropriate treatment and surveillance will be key to addressing the issues raised by imported infections. Identification of imported infections and carriage of organisms with antimicrobial resistance is critical. Once identified, effective infection control mechanisms exist for most infections. This should be a specific focus within the Public Health England surveillance strategy.

What is needed now?

- 2.10 This new Strategy responds to these challenges and identifies the future areas of activity that we need to focus on at a national and global level. It sets out the role of government and other organisations across the human and animal health, industry and research sectors in meeting the challenge and describes how the DH, PHE and Defra will co-ordinate work across these sectors to deliver a UK AMR programme.
- 2.11 The 'CMO's Annual Report'² also acknowledged that there are significant gaps in our knowledge and understanding of AMR. A substantial and extended research effort, with enhanced surveillance, will be needed to effectively support implementation and strengthen our modelling and forecasting capability so that there is a better understanding of the relative contributions of the inter-related factors that support the emergence and spread of resistance. Developing the evidence base is an important aspect of the work which will underpin this new Strategy and inform decisions that will enable us to make the greatest progress in addressing resistance.

3. The UK Commitment to Action

- 3.1 The UK fully recognises the importance of controlling AMR to protect public health and reduce the associated premature mortality and morbidity in as cost-effective a manner as possible. It is committed to an integrated approach to tackle AMR as part of the 'One-Health' approach¹ at national and international levels and to using its powers to provide the necessary leadership, stewardship and strategic direction for the NHS and the wider health and care system. It will do this by holding national bodies to account and ensuring that different parts of the system work properly together to improve clinical practice and patient outcomes.
- 3.2 In view of the global nature of the challenge and the real threat to our future health and prosperity, the government is working internationally to promote the importance of containing AMR. This includes influencing the EU regulatory landscape, especially new animal health law. In addition, it is encouraging accelerated progress on implementation of the '2001 WHO Global Strategy on the Containment of AMR'⁷ and '2011 EU AMR Strategic Action Plan'.³
- 3.3 More widely, the UK is actively supporting the WHO's global leadership role in addressing AMR. To this end, the Secretary of State for Health, on behalf of the UK, called for international action to tackle AMR at the 'Sixty-sixth World Health Assembly'¹³ held in May 2013. The UK and Sweden jointly hosted a side event¹⁴ at this meeting to raise awareness of AMR and the need for more co-ordinated international action.
- 3.4 The UK is helping to shape thinking on the issue and helping develop an international framework of action to harness contributions from all sectors and encourage collaborative working. The UK used its presidency of the G8* in June 2013 to host a meeting of G8 Science Ministers where AMR was discussed.¹⁵ It was agreed that AMR is a priority issue that demands an urgent global cross-sectoral response and research to better understand the origin, spread, evolution and development of resistance. The UK is also supporting work on AMR that will be considered at the 'World Innovation Summit for Health'¹⁶ in Doha in December 2013.
- 3.5 The CMO has recommended that the UK commits more widely to improving containment of AMR and infectious diseases by including AMR, for the first time, on the UK's 'National Security Risk Assessment'. This is being given active consideration, with Cabinet Office.
- 3.6 Ongoing development of the UK's research and development capacity as part of the BIS Office for Life Sciences work will be important, together with work with industry to explore innovative mechanisms to stimulate the development of new antimicrobials and rapid diagnostics for infections. It will also be important to determine the impact of

* The Group of Eight (G8) is a forum for the governments of eight of the world's eleven largest national economies. Members are Canada, France, Germany, Italy, Japan, the Russian Federation, the United Kingdom and the United States. The European Union is also represented. The UK assumed the one-year Presidency of the G8 in January 2013.

voluntary initiatives to reduce antibiotic use in animals and contribute to European discussions on the appropriate use of antibiotics in animals.

- 3.7 The National Institute for Health Research (NIHR) provides the framework through which DH positions, maintains and manages research including the research infrastructure of NHS England, as a national research facility. Up to £4 million has been allocated for a NIHR Health Protection Research Unit on AMR and Health Care Associated Infections (HCAI) from April 2014. The evidence base on AMR will also be strengthened by funding key research proposals, through the NIHR AMR themed call, and by encouraging better collaborations between life sciences companies and the NIHR clinical research infrastructure via the NIHR Office for Clinical Research Infrastructure (NOCRI).

Strategic Aims and Approach

- 3.8 As the CMO's Annual Report² identifies, the existing evidence clearly shows that as more antibiotics are used, selection of resistant organisms occurs. This, coupled with a paucity of new antimicrobials being developed, means the issue is reaching crisis point. Linked to the need to conserve and make more effective use of our existing antibiotics is the need to develop new approaches for hard-to-treat infections. Improved clinical practice will require changes in attitudes, behaviours and beliefs about antibiotics at a societal level. Given these factors, the overarching goal of this Strategy is to slow the development and spread of AMR by focusing on the following 3 strategic aims to:

- i. **improve the knowledge and understanding of AMR** through better information, intelligence, supporting data and developing more effective early warning systems to improve health security,
- ii. **conserve and steward the effectiveness of existing treatments** through improving infection prevention and control and development of resources to facilitate optimal use of antibiotics in both humans and animals,
- iii. **stimulate the development of new antibiotics, diagnostics and novel therapies** by promoting innovation and investment in the development of new drugs and ensuring that new therapeutics reach the market quickly.

- 3.9 These aims will be underpinned by actions in 7 key areas, which have been informed by the '2011 EU AMR Strategic Action Plan',³ and address the 3 recommendations set out in the 'CMO's Annual Report'.²

The 7 key areas for future action

- 3.10 The UK's commitment to tackle AMR and response to the actions requested in the '2011 EU AMR Strategic Action Plan'³ and '2012 EU Council Conclusions'⁸ will focus on the following 7 key areas for future action:

- 1 **improving infection prevention and control practices** in human and animal health, both through enhanced dissemination and implementation of best practice and better use of data and diagnostics (supports strategic aims i and ii),

- 2 optimising prescribing practice** through implementation of antimicrobial stewardship programmes that promote rational prescribing and better use of existing and new rapid diagnostics (supports strategic aims i and ii),
- 3 improving professional education, training and public engagement** to improve clinical practice and promote wider understanding of the need for more sustainable use of antibiotics (supports strategic aims i and ii),
- 4 developing new drugs, treatments and diagnostics** through better collaboration between research councils, academia, industry and others; and by encouraging greater public-private investment in the discovery and development of a sustainable supply of effective new antimicrobials, rapid diagnostics, and complementary tools for use in health, social care, and veterinary systems (supports strategic aims ii and iii),
- 5 better access to and use of surveillance data** in human and animal sectors through new arrangements that facilitate greater consistency and standardisation of the data collected across the system and encourage improved data linkage (supports strategic aims i and ii),
- 6 better identification and prioritisation of AMR research needs** to focus activity and inform our understanding of AMR. This may identify alternative treatments to new drugs as well as new or improved rapid or point-of-care diagnostic tests for humans and animals (supports strategic aims i, ii and iii),
- 7 strengthened international collaboration** working with and through a wide range of governmental and non-governmental organisations, international regulatory bodies and others to influence opinion, galvanise support, and mobilise action to deliver the scale of change needed globally (supports strategic aims i, ii and iii).

Details of specific actions necessary under each of these key areas are set out in the next chapter.

4. The 7 Key Areas for Future Action

- 4.1 To have maximum impact, collective action is needed by many partner organisations addressing each of the 7 key areas.

Key area 1: improving infection prevention and control practices

- 4.2 High standards of infection prevention and control will remain crucial to minimise the risk of infection, limit the emergence and spread of multi-drug resistant organisms in human and animals. As infections do not respect borders, infection control needs to be addressed both nationally and internationally.
- 4.3 For example, the significant fall seen in recent years, across the UK, of MRSA bloodstream infections and improvement in hand hygiene illustrates that with concerted effort, it is possible to significantly reduce infections, which in turn reduces the need for prescription of antibiotics. We now need to build on this success by adapting and embedding good practice in a way that takes account of the changing resistance patterns. Particular national and international attention is needed on Gram-negative organisms like *Klebsiella* species, where resistance to critical antibiotics is emerging and spreading.
- 4.4 Good farm management, bio-security, and animal husbandry systems underpin the health and welfare of food-producing animals. When applied appropriately they minimise disease, reduce susceptibility to bacterial disease and minimise the need for antibiotic use in animals.

Key area 2: optimising prescribing practice

- 4.5 Indiscriminate or inappropriate use of antibiotics is a key driver in the spread of antibiotic resistance. There is already an extensive range of guidance, education, tools and industry-sponsored initiatives to promote the responsible use of antibiotics in patients and animals, but most prescribing is carried out in the absence of adequate information about the nature of the infection or before the results of diagnostic testing are available.
- 4.6 Conserving the use of currently available antimicrobials is a vital part of antimicrobial stewardship. Whilst timely and appropriate treatment of probable bacterial infection is essential, we equally need to ensure use of the right drug, right dose at the right time and for the right duration to limit unnecessary antibiotic exposure.
- 4.7 Genomic technologies have potential to provide a valuable means to improve appropriate, prompt, patient treatment. In the next few years, whole genome sequencing and other diagnostic technologies will move from research laboratories into widespread use, enabling rapid identification of bacterial, viral and fungal pathogens and their genetic potential for drug resistance. This will help the early tailoring of treatment, benefitting both the patient and helping the conservation of antibiotics.

Key area 3: improving professional education, training and public engagement

- 4.8 To deliver in key areas 1 and 2 above, some specific actions are needed to maintain and raise awareness of optimal prescribing. Health Education England (HEE) has already made a commitment to ensure that infection control is part of all its funded courses but we need to do more to build clinical capability and deliver effective antimicrobial stewardship. Clinicians involved in prescribing need to remain up to date with emerging evidence on resistance and appropriate antibiotic usage. One way to help clinicians achieve this is by ensuring that continuing professional development programmes include the competences required for effective antibiotic stewardship.
- 4.9 Patients frequently believe, incorrectly, that antibiotics will help them recover from all respiratory tract infections faster. In addition, studies have shown¹⁷ that up to 25% of patients in England do not finish their course of antibiotics or keep them for later use, all practices that encourage AMR.
- 4.10 Patient consultations can be difficult when patients expect antibiotics for self-limiting infections. More needs to be done to educate patients and the public more generally about appropriate antibiotic use. Evidence on the benefits of informing patients about unnecessary antibiotic use is available. Resources for GPs like 'Treat Antibiotics Responsibly, Guidance and Education Tool' (TARGET)¹⁸ and 'Stemming the Tide of Antibiotic Resistance' (STAR),¹⁹ together with local initiatives including the use, by some GPs, of non-prescription pads and delayed antibiotic prescribing (whereby patients are asked to use the prescription only if they do not get better) have helped reduce the number of prescriptions dispensed. These approaches should be used more widely. Similarly, animal keepers need to understand and follow directions for correct drug administration.
- 4.11 Public and professional awareness-raising and educational activities, like the annual 'European Antibiotic Awareness Day' (EAAD)²⁰ need to continue to remind both the public and professionals of the need to use antibiotics appropriately and help drive further improvements in clinical prescribing practice.

Key area 4: developing new drugs, treatments and diagnostics

- 4.12 Whilst it is essential that we should do all we can to conserve the effectiveness of existing antimicrobials, it is also important to ensure that we have effective treatments available for the future, not only new antibiotics but also vaccines and other therapeutic approaches for humans and animals. Human and veterinary rapid diagnostics are urgently needed to help differentiate between bacterial and viral infections, as well as to enable fast identification of highly-resistant strains. Technologies like whole genome sequencing must also be exploited to help increase our ability to investigate the epidemiology of bacterial outbreaks. In addition to health benefits, improved diagnostics and new therapeutics will contribute to UK economic growth by promoting inward investment and job creation in the UK's research infrastructure. It is important to act now to ensure we have a sustainable supply of effective treatments in the future.
- 4.13 The discovery and development of new drugs takes time (about 10 to 15 years) and a barrier to developing new antibiotics is their relatively low commercial return on investment, relative to investments in other therapeutic areas. This low return on investment is driven by:

- scientific difficulty of finding new agents,
- risk of inadequate return on investment given that duration of drug use is limited compared to drugs for chronic conditions,
- concerns over the cost and complexity of the regulatory approval process,
- uncertainty about the regulatory environment for new antimicrobials.

- 4.14 There is a need to do more to address the commercial viability and market failure issues that are hampering investment in antibiotic development. Approaches to facilitate the regulatory pathways for new antibiotics and to provide new incentives for research and development are reported in the academic literature.^{21, 22, 23}
- 4.15 Work to reform and harmonise regulatory regimes relating to the licensing and approval of antibiotics, especially clinical trial requirements, is also needed. The EU law that concerns the assessment and authorisation of new veterinary medicines is currently under revision. Regulatory uncertainty is dissuading pharmaceutical companies from developing new antimicrobial products for veterinary use. Pharmaceutical companies have expressed concern that potential new controls and additional data requirements may limit the market for any new products and thus limit return on investment.
- 4.16 Equally important is the research and development of novel approaches to the treatment and prevention of infections. This includes using substances to strengthen the immune response to bacterial infection, such as pre and probiotics. Naturally occurring bacteriophages, their enzymes and vaccines are already under consideration. To maximise progress in this area it will be important for industry and academia to work together to accelerate discovery and development through well regulated research. We recognise that the development of these may, in some instances, involve research involving animals where no alternative exists. The relevant Research Councils, industry and third sector should work together to establish a range of new mechanisms, including the use of consortia, to facilitate greater collaborative working.

Key area 5: better access to and use of surveillance data

- 4.17 Surveillance data that focus on bacterial resistance, the epidemiology of bacterial infections, drug utilisation and clinical outcome are essential to monitor resistance trends. These data will help assess the impact of rational prescribing programmes for both current and new antibacterial agents in humans and animals.
- 4.18 While surveillance programmes have improved dramatically in scope in recent years, information on the impact of antibiotic use on patient outcome and development of resistance is limited. Antibiotic prescription data for humans are only collected centrally for primary care. Work is underway to address these needs and strengthen surveillance arrangements. In addition, the drivers of veterinary prescribing practice are being explored to direct future activity aimed at minimising pressures that currently influence prescribing habits.
- 4.19 Better sharing of local, regional and national information and data on emerging issues in human and animal health together with use of early warning systems is needed to trigger appropriate containment measures to limit the spread of resistant organisms.

Key area 6: better identification and prioritisation of AMR research needs

- 4.20 Identification and prioritisation of research needs to help both academics and research funders ensure that key questions are addressed. There are a number of funding streams and initiatives that are currently funding research on AMR. These include the UK CRC 'Translational Infections Research Initiative',²⁴ the 'Health Innovation Challenge Fund',²⁵ the NIHR themed 'call for action'²⁶ which is described more fully in paragraph 5.5 and research through the NIHR healthcare associated infection and AMR unit.
- 4.21 Further fundamental research is also underway through the Medical Research Council (MRC) Centre for Molecular Bacteriology and Infection, established in July 2012 with a unique focus on the study of disease causing bacteria, to understand better the molecular basis of the emergence and spread of AMR.²⁷ In addition, the Biotechnology and Biological Sciences Research Council (BBSRC)²⁸ provides ongoing support for research activities with a focus on AMR, including EU-level co-ordination.
- 4.22 We are aware of evidence gaps in some areas. For example, research is needed to provide a more detailed understanding of the significance of different transmission pathways between the environment, humans, animals and the food supply chain in promoting transfer or increase of resistance in human and veterinary pathogens, so we can target and prioritise our interventions appropriately to minimise resistance.
- 4.23 Research is also needed to develop new technologies, including human and veterinary rapid diagnostic tests to differentiate between bacterial and viral infections, enable fast identification of the organisms causing disease, and to identify high-risk strains and their resistance. To reduce reliance on broad-spectrum drugs, tools are also needed to help with treatment and disease control, and to develop alternative approaches, including strategies that do not rely on traditional antibiotics. This should be complemented with further research on combination therapy and optimal dosing with currently available antibiotics.

Key area 7: strengthened international collaboration

- 4.24 AMR is a global problem and needs concerted global action to tackle it. Whilst there is increasing recognition of the challenge of AMR, more can be done at an international level to raise awareness of the issues and co-ordinate strategic approaches. The UK is playing a leading role in influencing European and international thinking, seeking support, securing commitments to prioritise the issue and mobilising action to deliver the scale of change needed. The UK has already raised the profile of the issue at an international level and is making it everyone's business, securing commitments to further action, harnessing contributions from all sectors and encouraging collaborative working, and is committed to taking collective action on the priority issues.
- 4.25 More joint initiatives like the 'EU /USA Transatlantic Task Force on AMR' (TATFAR),²⁹ and the 'European Research Network, ERA-NET Scheme',³⁰ are also needed to help foster a culture of data and technology sharing/transfer between animal and human health fields. These should also encourage innovative approaches to develop rapid diagnostics, new antibiotics and novel therapies as well as encourage greater research collaboration. The European Commission has put in place mechanisms like:
- research programmes eg the EU 'Framework Programme (FP7) for Research and Technological Development',³¹ and its successor, 'Horizon 2020',³²

- the ‘Innovative Medicines Initiative’ (IMI),³³
- the Joint Programming initiative on Antimicrobial Resistance³⁴ (18 countries working to rationalise the European research efforts in AMR with the UK represented by MRC),
- the EU ‘co-ordinated surveillance networks’[♦]
- the ‘Early Warning Response System’ (EWRS)³⁵ to facilitate routine AMR data collection,
- risk assessments alerting Member States urgently to significant resistant infections,
- and finally, the ‘European Antibiotic Awareness Day’ (EAAD)²⁰ public education campaign,

which all help.

Together, these initiatives provide an opportunity for the UK to share data and experience for our mutual benefit and enable UK scientists to become actively involved in EU initiatives without duplicating work required at a national level. These are all important strands of work which must continue, but the pace in some areas needs to be accelerated if they are to have a significant impact.

- 4.26 Increased collaborative working is similarly needed at a global level to encourage innovation in the development of new antimicrobial agents, diagnostics and multi-disciplinary collaborations between researchers working on AMR in humans, animals and the environment under the ‘One-Health’ approach.¹ This needs to be supplemented by work to review the regulatory framework, international standards and resolutions to contain antibiotic use, reduce sub-optimal prescribing of antimicrobials, strengthen data collection and analysis systems to provide comparable human and animal information, and make better use of prescribing and sales information.

Action in these 7 key areas

- 4.27 The overarching actions that need to be taken in each of the 7 key areas are set out in Annex B. Responsibility for delivery of those is necessarily spread across and between sectors. The contribution that various sectors should make to each overarching action area is set out in Chapter 5:

- the Human Health and Social Care Sector,
- livestock, Food Retail and Veterinary Sectors,
- research Councils, other research funders and academics,

♦ The 4 EU surveillance networks are: European Antimicrobial Resistance Surveillance network (EARS - net), which collects resistance information on key bacteria, European Surveillance of Antibiotic Consumption network (ESAC), which monitors antibiotic consumption in primary and hospital care; European Surveillance of Veterinary Antimicrobial Consumption project (ESVAC), which collects information on how antimicrobial medicines are used in animals, the European Food Safety Authority EU Summary Report for Antimicrobial Resistance.

- pharmaceutical Industry,
- other organisations.

5. Meeting the Challenge

- 5.1 This is an ambitious work programme. The UK government cannot deliver the action necessary to minimise the spread of AMR on its own. Success will require a wide range of public and private sector bodies to take co-ordinated action to deliver an integrated programme, which will safeguard human and animal health.
- 5.2 This chapter describes the constitution and types of activities each sector is being asked to make to help deliver the overarching actions detailed in Annex B. They are broadly grouped under the 3 strategic aims of the Strategy.

The Human Health and Social Care Sector

- 5.3 Public Health England (PHE), NHS England, clinical commissioning groups, Health Education England (HEE), the Medicines and Healthcare products Regulatory Agency (MHRA), National Institute for Health and Care Excellence (NICE), Food Standards Agency (FSA) and other health sector agencies and their equivalents in the devolved administrations and Local Authorities, together with providers of health care and social care services, need to take action to:

improve the knowledge and understanding of AMR by:

- incorporating antimicrobial resistance awareness, responsible prescribing, dispensing and administration practice, as well as effective prevention, management and control of infection in undergraduate and postgraduate curricula for human medicine, nursing, pharmacy, dentistry and other professionals,
- continuing to raise awareness of AMR issues and participate in the 'European Antibiotic Awareness Day'²⁰ each year,
- finding ways to raise awareness, increase public engagement and encourage societal changes in behaviour.

conserve and steward the effectiveness of existing treatments by:

- ensuring adherence to evidence-based guidance on interventions that aim to change behaviour and professional practice, including improving the uptake of NICE guidance throughout the NHS,
- auditing prescribing practices and outcomes across the system to assess the effects of antimicrobial stewardship programmes in human settings,
- providing clinical leadership and improved collaborative working, between senior management and infection prevention and control teams, by prioritising antimicrobial stewardship and adherence to best practice in infection prevention and control, in both active and preventative treatment regimes,
- encouraging wider use of interventions to support appropriate antibiotic prescribing, like the 'Start Smart-Then Focus'³⁶ guidance on antibiotic stewardship in hospitals and the use of resources like 'TARGET',¹⁸ 'STAR'¹⁹ produced for GPs as well as considering the wider use of delayed prescribing

practices and exploring how to encourage patients to use community pharmacies for advice,

- developing and implementing effective antimicrobial stewardship quality measures, a quality standard on antimicrobial stewardship and guidance on heterogeneity of prescribing in both secondary and primary care,
- increasing the use of point-of-care diagnostics to identify where antimicrobials are required, as well as to reassess the appropriateness of the diagnosis and treatment,
- extending the learning from hospital antimicrobial stewardship programmes and prescribing measures to primary care by developing tools to facilitate behaviour changes like mobile downloadable and readable applications that can be linked to NICE and NHS Evidence,
- improving surveillance and early warning systems and developing information standards for national surveillance of infections whilst promoting local use of information,
- identifying the optimum arrangements for recording and reporting of data (including the use of electronic prescribing) as well as analysis of data on antibiotic use, resistance and clinical outcomes,
- improving the quality and standardisation of routine antibiotic testing and interpretation of results to improve diagnosis and treatment of infections, exploring linkage of human and veterinary data and consideration of sharing laboratory/ testing methods between the sectors,
- using the 'Innovation, Health and Wealth' report to accelerate the adoption of innovation in the NHS.³⁷

stimulate the development of new antibiotics, diagnostics and novel therapies by:

- preparing to take advantage of genomic technologies and developments in point-of-care diagnostics in the NHS and by independent sector providers of healthcare, microbiology and virology services,
- implementing new immunisation programmes as recommended by the Joint Committee on Vaccination and Immunisation (JCVI),³⁸ improving vaccination coverage by those groups with traditionally low uptake and promoting development of new vaccines including those used against multi-drug resistant organisms.

Livestock, Food Retail and Veterinary Sectors

5.4 Veterinary surgeons and nurses and their professional bodies, including the Royal College of Veterinary Surgeons (RCVS) and the British Veterinary Association (BVA), animal keepers and their representative bodies together with trade associations and food retailers need to take action to:

improve the knowledge and understanding of AMR by:

- embedding an appreciation of AMR issues and strategies for containing resistance in undergraduate courses,
- considering influencing uptake of training through statutory professional standards, for example, for veterinary surgeons by inclusion in the 'RCVS Day-One Competency Framework'³⁹ and/or through the annual continuing

professional development (CPD) requirements necessary to retain membership of the RCVS or other professional body,

- increasing the level of provision of targeted CPD for veterinary professionals,
- increasing access to relevant training for animal keepers,
- continuing to expand activities aimed at raising awareness and encouraging behaviour change by veterinary and farming associations, for example, through use of farming sector events and trade publications to disseminate responsible use messages, and by concerted active participation across all relevant groups in the 'European Antibiotic Awareness Day',²⁰
- facilitating development of sector-specific prescribing guidelines and promoting responsible use practices, including effective dissemination of guidance.

conserve and steward the effectiveness of existing treatments by:

- improving adherence to responsible prescribing and responsible administration principles for antibiotics by ensuring provision of practice prescribing policies and by dissemination of education material aimed at aiding compliance with medication instructions,
- encouraging animal keepers to work closely with their veterinary surgeons to prioritise diagnosis of disease in livestock and companion animals, and to encourage early use of appropriate diagnostic testing, in particular, bacterial culture and sensitivity tests,
- encouraging livestock farmers to adhere to government guidance on bio-security, animal husbandry and on farm health planning for each of the major farming sectors and to take proactive action to reduce the risk of disease occurring in their animals,
- considering the use of 'farm assurance schemes' as a mechanism to increase adherence to best husbandry including isolation of sick animals, testing of new stock and responsible use of antibiotic principles, while ensuring animal health and welfare,
- encouraging retailers to review their standards for meat and animal products and to set clear specifications, concerning bio-security, antimicrobial stewardship and good husbandry throughout the supply chain for overseas as well as nationally sourced UK meat and animal products, working with suppliers and veterinarians to ensure compliance,
- working collaboratively to strengthen the available evidence base, in particular through the collection and sharing of surveillance and usage data needed to benchmark current levels of resistance and antibiotic consumption and improve early warning systems at national and global levels,
- continuing to explore options for the collection and analysis of veterinary medicine prescription data, including the use of local audit,
- encouraging the research needed to gain a greater understanding of the impact of interventions intended to minimise development and spread of antibiotic resistance,

- ensuring that any new data-collection initiatives use methodologies and analytical techniques that harmonise with on-going EU-led projects, to maximise their potential to enhance the wider evidence base.

Research Councils, other research funders and academics

5.5 The Research Councils, other funders and academics need to collaborate to ensure that research needs to continue to be identified as the evidence base evolves and that key priorities are funded,

improve the knowledge and understanding of AMR by:

- responding to the ‘NIHR call for AMR research’²⁶ in autumn 2013, with proposals to increase the evidence base in the areas of better prevention, improved surveillance and monitoring and diagnosis as well as the more effective use of existing antibiotics, improved education and training and the development of new antimicrobial therapies and better treatment strategies,
- developing AMR research capability in the following areas:
 - novel approaches to surveillance and better integration of information infrastructure to determine the spread of infectious disease and resistance (including across species),
 - development and use of rapid diagnostics, including point-of-care diagnostics to avoid inappropriate treatment and reduce antibiotic misuse,
 - innovation in antimicrobial development and the provision of evidence for novel molecules to be developed into drugs.

conserve and steward the effectiveness of existing treatments by:

- exploring the possibility of developing a ‘drug resistance index’ to communicate gaps in antibiotic effectiveness to non-experts and help aggregate data on resistance to various drugs to assess trends in drug resistance over time and across locations,
- evaluating the effectiveness and consequences of strategies to increase heterogeneity in antimicrobial prescribing and the impact of rapid diagnostics as these are introduced.

stimulate the development of new antibiotics, rapid diagnostics and novel therapies by:

- developing new treatments for bacterial infections, from rigorous identification of new targets through to new approaches to treatment,
- contributing to European Union work to map what research is ongoing across Europe to help identify areas for further work,
- developing coalitions between academia and biopharmaceutical companies,

- working to improve diagnostic technology for infection and develop rapid diagnostics, which will allow movement away from broad-spectrum treatments to more tailored treatment approaches,
- utilising the ‘Innovative Medicines Initiative’ (IMI),³³ a joint undertaking between the European Union and the European pharmaceutical industry, which may facilitate more efficient discovery and development of better and safer medicines for patients,
- developing new lead structures for drug discovery projects in the public and private sectors supporting international initiatives to combat AMR, including developing drugs, diagnostics, innovative alternative therapies, combination therapy and optimal dosing regimens across human and veterinary sectors,
- promoting the development and uptake of genomic technologies relating to AMR, particularly as the price of genomic testing falls and its power increases.

Pharmaceutical Industry

- 5.6 Industry has a corporate and social responsibility to contribute to work to tackle AMR by finding ways of extending the life of antibiotics, making the supply of effective antibiotics sustainable, facilitating society in being better custodians of these valuable resources and using them optimally both now and the future.
- 5.7 Pharmaceutical, bio-pharmaceutical and diagnostics manufacturers and trade associations need to:

improve the knowledge and understanding of AMR by:

- supporting and providing resources for training and education of healthcare and other professionals,
- engaging in activities to increase awareness to effect behaviour change.

conserve and steward the effectiveness of existing treatments by:

- promoting the practice of responsible use through the responsible provision of medicines, for example, by making current veterinary antibiotics available in pack sizes that facilitate and encourage appropriate use.

stimulate the development of new antibiotics, rapid diagnostics and novel therapies by:

- improving collaborative working to ensure excellent science is developed and has a clear route for translation,
- developing a European product development partnership scheme for antimicrobial drugs,
- developing new treatments for all infections, particularly bacterial, from rigorous identification of new targets through to new paradigms for treatment,

- utilising the 'Innovative Medicines Initiative' (IMI), which may facilitate stimulating the development of new antibiotics, rapid diagnostics and novel therapies,
- developing new vaccines targeted at multi-resistant organisms,
- increasing involvement in genomic diagnostics and the improvement of companion diagnostics for drug development in this field.

Other organisations

5.8 In addition to the organisations listed above many other organisations have an important role in addressing antimicrobial resistance:

- local government can include infectious disease issues, infection control and antimicrobial stewardship in their 'Joint Strategic Needs Assessments' (JSNAs),⁴⁰
- Royal Colleges, professional bodies and learned societies can enhance understanding and knowledge sharing between academia, researchers and clinicians. These organisations are well placed to champion best practice with their members and other professional stakeholders, sponsoring events to raise awareness of infection prevention and control as well as antimicrobial stewardship, and can develop evidence based guidance on best practice in relation to:
 - detection, diagnosis and treatment of multi-drug resistant organisms
 - infection prevention and control
 - surveillance
 - prescribing
- expert scientific advisory committees and other government advisory bodies[▼] should continue to play a central role in identifying emerging issues. This will be achieved by information gathering, horizon scanning and risk assessment. In addition, they provide advice on infection prevention and control, outcome measures and research priorities.

[▼] The network of government expert scientific advisory committees and bodies include:

- the expert Advisory Committee on Dangerous Pathogens (ACDP),
- Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI),
- the Defra Antimicrobial Resistance Co-ordination (DARC) group,
- the Advisory Committee on Microbiological Safety of Food (ACMSF).

6. Implementation

- 6.1 Taken together, this package of activity, both current and proposed, provides the platform from which to garner greater support for urgent national and international action, changing the landscape on AMR so that it ceases to be the issue of concern that it is today. However, we do not underestimate the extent of the work that needs to be taken forward by our delivery partners and the community at large to facilitate the level of change in behaviour, custom and practice needed.
- 6.2 The government's role is therefore to lead and co-ordinate the work of various partners in the public and private sectors, acting as steward of the system. It also has an important role in stimulating wider public debate and innovation. A new interdepartmental UK High Level Steering Group (HLSG) will have a key role in ensuring delivery partners work together across the system and engage with private sector partners and industry, reporting progress to the Chief Medical Officer and Chief Veterinary Officer.
- 6.3 The multi-faceted and diverse nature of this work programme will require the involvement of a wide range of organisations to deliver it, raise awareness of the issues and create the necessary impetus to drive changes in attitude and behaviour at a societal level.
- 6.4 A programme of meetings will commence in the autumn 2013 to enable the sectors to discuss how to take work forward in their areas and consider progress.

The Interdepartmental High-level Steering Group (HLSG)

- 6.5 The Department of Health, with support from PHE and Defra, will lead the implementation of this Strategy as a comprehensive, integrated programme across government. This will be overseen by the UK HLSG, chaired and supported by the Department of Health (see Box 1). The group will be responsible for developing an agreed work programme across the sectors, with timescales for delivery of specific actions. It will also have a key role in ensuring that there is progress in implementing the Strategy across all sectors and that momentum is maintained.
- 6.6 The HLSG will be charged with:
 - developing a plan of work focusing on the actions in chapter 5 and Annex B, jointly agreed with key delivery partners, to be published before April 2014,
 - developing detailed outcome metrics (see paragraphs 6.11 and 6.12) which will be used to assess the impact of the measures taken to give effect to the Strategy in terms of delivering health protection improvements,
 - publishing an annual report on progress, outputs and outcomes of the work each November, commencing in 2014.
- 6.7 During the first 12 months, the work of the HLSG is expected to focus on developing the detailed implementation plan to take forward the Strategy, developing outcome

metrics as well as setting up the infrastructure and systems needed to collect the baseline surveillance data.

- 6.8 By the second year (2015) the HLSG will start to consider outputs from PHE's newly formed 'English Surveillance Programme for Antimicrobial Utilisation and Resistance' (ESPAUR) on resistance levels in critically-important bacteria, (ie those for which we have only a few antibiotics treatments remaining) which will help inform decisions on the most appropriate interventions needed.
- 6.9 By the third year (2016) there is expected to be sufficient data, intelligence and information available to assess whether the programme of work is on course to deliver the strategic objectives or whether the work programme needs adjusting.
- 6.10 At the end of the 5 year period (2018) an evaluation report will be produced which will assess the effectiveness of the implementation plan, identify any further priorities for action and make additional recommendations as necessary.

Measuring Outcomes

- 6.11 The HLSG will involve the network of scientific expert Advisory Committees in developing detailed outcome measures around the following areas:
 - trends in resistance in key bacterial human infections (Annex C),
 - improvement in public and professional knowledge and understanding of antimicrobials and their appropriate use,
 - improving the quality of prescribing in primary and secondary healthcare settings compared to the position in 2012, where baseline data is available,
 - monitoring the use of antibiotics in animals, specifically in relation to the WHO defined top 3 Critically Important Antibiotics (CIAs) in human medicine,⁴¹
 - strengthened global security through ensuring global alignment in addressing AMR.
- 6.12 Measures in the above areas will provide a means of assessing trends in resistance and to ensure the necessary progress is being made to control resistance in a way that avoids compromising clinical outcomes or other undesirable and unintended consequences.

Conclusions

- 6.13 We cannot undo the harm that has already been done, but more can be done to minimise further harm, reduce the risk of cross-infection and improve patient safety, animal health and welfare. AMR is a complex issue that requires a comprehensive and concerted effort to tackle it effectively.
- 6.14 If further gains are to be realised, clinicians, veterinarians and others healthcare professionals, senior managers and patient groups, will need to work in closer collaboration with industry. This will help to eliminate poor practice, improve antibiotic prescribing and administration; guide and develop new approaches to the future management of infectious disease.
- 6.15 The comprehensive programme of work set out in this Strategy, if implemented effectively, will deliver significant improvements in the way AMR is addressed, provide

a solid foundation to bring about some fundamental changes in approach and capability that will extend beyond the 5 year term.

Box 1 High Level Steering Group (HLSG) organisations and their responsibilities

The Department of Health (DH)

The DH will have overall responsibility, on behalf of the UK government, for ensuring delivery of the AMR programme commitments, including co-ordinating cross-government engagement and providing support to the HLSG. In addition, DH will have particular responsibility for leading work to:

- better identify and prioritise research,
- stimulate the development of new drugs, treatments and diagnostics,
- strengthen international collaboration,
- improve the analytical evidence base.

The Department for Environment, Food and Rural Affairs (Defra)

Defra will have overall responsibility for co-ordinating cross-government activity relating to delivery of the animal health aspects of the AMR programme for the UK. Joint working with PHE, DH and other relevant partners will be required on aspects relating to the human-animal interface, on identification and prioritisation of research, drug development needs and the analytical evidence base. Defra will be responsible for leading the animal health aspects of government AMR work, bringing together relevant partners to:

- improve infection prevention and control practices,
- optimise prescribing practice,
- improve professional education, training and public engagement,
- ensure better access to and use of surveillance data.

The Department for Business Innovation and Skills (BIS)

BIS has a role in ensuring that the relevant areas of the Strategy are aligned with the 'Strategy for UK Life Sciences'⁴² and the government's wider industrial Strategy. BIS is also responsible for sponsorship of the Research Councils, as described in Box 2.

The Devolved Administrations (DAs)

The DAs have developed or are developing national AMR strategies/action plans. Annual reports on progress in delivering those strategies will form the basis of their contribution to delivering the wider UK Strategy.

Public Health England (PHE)

PHE, jointly working with the Devolved Administrations equivalent public health and health protection organisations, will have overall responsibility for co-ordinating cross-government activity relating to delivery of the human health aspects of the AMR programme for the UK. Joint working with Defra and other relevant partners will be required on aspects relating to the human-animal interface. PHE will be responsible for leading the human health aspects of AMR work, bringing together relevant partners to:

- improve infection prevention and control practices,
- optimise prescribing practice,
- improve professional education, training and public engagement,
- ensure better access to and use of surveillance data.

NHS England

NHS England, working jointly with the NHS and the Devolved Administrations, will support work to improve antimicrobial resistance surveillance and infection prevention and control in the NHS, for example through improved use of surveillance data, improved recording of clinical information and adherence to guidance to improve the quality of prescribing in both primary and secondary care.

The National Institute for Health and Care Excellence (NICE)

NICE will work with other delivery partners to consider the development of comprehensive evidence based antimicrobial prescribing guidance for primary and secondary care, supporting work to encourage responsible use of antibiotics, improving professional knowledge and clinical practice with respect to antimicrobial stewardship.

Health Education England (HEE)

HEE, working jointly with equivalent organisations in the Devolved Administrations, will lead improvement in the education and training of healthcare workers and have a role in helping strengthen curricula on antimicrobial resistance, responsible prescribing, infection prevention and control and develop e-learning tools to support this.

The Medicines and Healthcare products Regulatory Agency (MHRA)

The MHRA will continue to develop guidance to help make clinical trials as effective as possible and helping companies through the regulatory procedure. MHRA will take an active role in supporting the development of a new business model for drug development and furthering work at an international level to address this issue.

Box 2 Research Councils

The Research Councils fund basic underpinning, applied and translational research in the area of antimicrobial resistance. Training in disciplines like bacteriology and clinical microbiology is supported through Fellowship schemes. The Medical Research Council (MRC) has an important role in funding basic and translational research in the areas of microbial pathogenesis, AMR and the development of new antimicrobials. It also supports Fellowship schemes to develop capability in bacteriology and clinical microbiology, and funds the MRC Centre for Molecular Bacteriology and Infection. MRC represents the UK in the 'European Union Joint Programming Initiative on AMR'³⁴ to streamline the European research effort in the area.

The Biotechnology and Biological Science Research Council (BBSRC)²⁸ has an important role in funding basic and applied research and training in animal health, microbiology and genetics, including understanding AMR, development of novel antimicrobials, and development of alternative approaches, including vaccines and breeding for disease resistant animals. BBSRC is working with other National, European and International partners to fund research that will address not only basic understanding of antimicrobial resistance but also alternatives to current antimicrobials and anthelmintics used to treat disease in agricultural animals.

Consultees and Respondents

Responses to the October 2012 'technical engagement exercise' were received from around 140 bodies (listed below) including a number from individuals and professionals employed by one of the bodies.⁴³

Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)	All Wales Medicines Strategy Group
All Wales Prescribing Advisory Group	Animal Health and Welfare Board for England
Advisory Committee on Microbiological Safety of Food (ACMSF)	Antibiotic Action
Association of British Healthcare Industries (ABHI)	Association of Pharmaceutical Industries (ABPI)
Bart's Healthcare	Bella Moss Foundation
Bill and Melinda Gates Foundation	Biotechnology and Biological Sciences Research Council (BBSRC)
British Dental Association	British Equine Veterinary Association
British Generic Manufacturers Association (BGMA)	British Infection Association (BIA)
British In Vitro Diagnostics Association (BIVDA)	British Pig Veterinary Association/Pig Veterinary Society
British Retail Consortium	British Small Animals Veterinary Association
British Society of Antimicrobial Chemotherapy (BSAC)	British Thoracic Society
British Veterinary Association (BVA)	British Veterinary Poultry Association
<i>C. diff</i> support	Care Quality Commission
Chemical Biology Ventures	Defra Antimicrobial Resistance Co-ordination Group (DARC)
Defra - VMD	Defra UKZADI
Department for Business Innovation and Skills (BIS)	Department for Business Innovation and Skills (BIS) GO Science
Department for Business Innovation and Skills (BIS) Office for Life Sciences	Department For International Development (DFID)
Department of Health	DHSSPSNI (Department of Health and Social Security and Public Safety Northern Ireland).
Directors of Public Health (DsPH)	European Centre for Disease Prevention and Control (ECDC)
Economic and Research Council (ESRC)	Elanco Animal Health – Corporate member of NOAH
Ethical Medicines Industry Group (EMIG)	Europe Association of British Healthcare Industries
Faculty of Public Health	Fish Veterinary Society (FVS)
Food and Drinks Federation	Food Standards Agency (FSA)
Food Manufacturers Federation (Health Food Manufacturers Association-HFMA)	Frimley Park Hospital NHS Foundation Trust
Galderma UK and Ireland Ltd– Prescription Division	HAI Task Force groups - Scotland
Harrogate District Hospital NHS Trust	Health and Social Care in Northern Ireland (HSCNI)
Health Protection Agency (HPA), now PHE	Health Protection Scotland (HPS)
Healthcare Infection Society (HIS)	ICNet
Imperial College London	Infection Prevention Society (IPS)
Infectious Disease Research Network	Johnson and Johnson Medical Ltd
Leeds Teaching Hospital NHS Trust	Local Government Association (DPH)
London School of Hygiene and Tropical Medicine (LSHTM)	Medical Research Council (MRC)

Medicine and Healthcare products Regulatory Agency (MHRA)	Ministry of Defence (MOD)
Milton Keynes Community Health services	MRSA Action
Monitor	National Farmers Union
National Concern for Healthcare Infections	National Office of Animal Health (NOAH)
National Institute for Health and Care Excellence (NICE)	National Voices
National Pharmacist Association	Norgine Pharmaceuticals Ltd
NHS HAI Executive Leads – Scotland	Patients Association
Oxford Health NHS Foundation Trust	RAND Europe
Public Health Wales	Roslin Institute
Responsible Use of Medicines in Agriculture Alliance (RUMA)	Royal College of Nursing (RCN)
Royal College of General Practitioners (RCGP)	Royal College of Physicians (RCP)
Royal College of Pathologists (RCPATH)	Royal Pharmaceutical Society (RPS)
Royal College of Veterinary Surgeons (RCVS)	Royal Veterinary College
Royal United Services Institute (RUSI)	Science and Technology Facilities Council
Sanger Institute / University College London	Scottish Antimicrobial Prescribing Group
Scottish Government Directorate for Health and Social Care	Scottish Infection Research Network (SIRN)
Scottish Infection Prevention Network	Scottish Government Directorate for Agriculture, Food and Rural Communities
Scottish Microbiology and Virology Network	Scottish Directors of Pharmacy
Scottish Directors of Public Health	Society of Chiropractors and Podiatrists
Sheep Veterinary Society	The Soil Association
The International Scientific Forum on Home Hygiene	UK Clinical Pharmacist Association (UKCPA)
The Technology Strategy Board	Vetpol Ltd
UK Zoonoses Animal Diseases and Infections Group (UKZADI)	Welsh Government
Various Experts from Academia	Chief Executive of HSC Trusts
Northern Ireland consultees:	Chief Executive of HSC Board
Chief Executive of PHA	Chief Executive of BSO
Chief Executive of PCC	Chief Executive of RQIA
Chief Executive of NIAS	Assistant Director of Public Health (Health Protection), Public Health Agency
Executive Medical Director/Director of Public Health, Public Health Agency (<i>for distribution to relevant public health staff</i>)	Director of Research and Development, Public Health Agency
Director of Nursing and AHPs, Public Health Agency	Heads of Pharmacy and Medicines Management, HSC Trusts
Assistant Director of Integrated Care, Pharmacy and Medicines Management, HSC Board	Family Practitioner Service Leads, HSC Board
GP Medical Advisers, HSC Board	Medicines Management Advisers
Medical Directors, HSC Trusts	Medical Director, NI Ambulance Service
Nursing Directors, HSC Trusts	Regulation and Quality Improvement Authority (RQIA)
Microbiology Standing Specialist Advisory Group in Wales	

Overarching Actions Needed in the 7 Key Areas

The following are the overarching actions required in each of the 7 key areas. The detailed contribution that each of the sectors can make to delivery of these actions is described in Chapter 5.

Key area 1: improving infection prevention and control practices

Actions needed to further improve infection prevention and control in human and animal systems are:

- embedding strong infection prevention practices and control of cross-infection in all educational programmes for healthcare workers and veterinary teams,
- ensuring adherence to evidence-based guidelines for preventing healthcare associated infections and clinical best practice guidance for infections caused by managing multi-drug resistant organisms,
- encouraging and supporting animal keepers to improve bio-security and husbandry practices to minimise disease occurrence; for example, through appropriate housing design and good disinfection procedures,
- encouraging appropriate use of best practice in disease control, for example through isolation of sick animals, testing of new stock prior to mixing, use of vaccines and disease eradication programmes,
- sharing intelligence on emerging issues in human and animal health; as well as making better use of early warning systems to trigger appropriate containment measures at a national and global level to limit spread of AMR,
- cost-effective use of licensed vaccines to reduce the incidence of infections as well as promotion of the development of new vaccines, including those against multi-drug resistant organisms.

Key area 2: optimising prescribing practice

Actions needed to further improve antimicrobial conservation and stewardship through optimising prescribing practice are:

- developing enhanced education and training in prescribing and administration of antibiotics,
- identifying the optimum arrangements for recording and reporting of data (including the use of electronic prescribing), as well as analysis of data on antibiotic use, resistance and clinical outcomes,

- improving the quality and standardisation of routine antibiotic testing and interpretation of results to improve diagnosis and treatment of infections,
- evaluating the effect of reasonable innovative strategies to increase heterogeneity of local antibiotic prescribing policies over set periods of time on usage, resistance rates and outcomes,
- auditing local prescribing practices and outcomes across the system to assess the effects of antimicrobial stewardship programmes in human and animal settings,
- facilitating development of sector specific prescribing guidelines, which, for example advocate minimising the routine use of preventative antibiotics in animal health and to promote responsible use practices including engaging with representatives across the animal health spectrum to ensure effective dissemination of guidance.

Key area 3: improving professional education, training and public engagement

Actions needed to improve education, training and engagement are:

- identifying mechanisms to improve the uptake of guidance for professionals, including through commissioning and audit of prescribing, infection prevention and control,
- development of NICE quality standards,
- ensuring that generic prescribing competences, which are being developed, are adopted and embedded in curricula, and that antimicrobial stewardship competences are included in professional curricula and continuing professional development,
- increasing public engagement to promote key messages about antimicrobial use, including promotion of training of non-health professionals, like farmers, with responsibility for administering antibiotics,
- facilitating public debate to shift the societal view to raise awareness of antibiotics and ways to limit their use. This could include considering the potential for restricting the use of antibiotics for low risk self-limiting infections and/or restricting antibiotic use more widely to affect behaviour change.

Key area 4: developing new drugs, treatments and diagnostics

Actions needed to accelerate the discovery and development of new drugs, vaccines, rapid diagnostics and treatments are:

- encouraging innovation and providing an impetus for improved collaborative action to develop rapid diagnostics and new treatments and vaccines,
- supporting innovation through development of the scientific infrastructure, for example, through the BIS 'Strategy for UK Life Sciences',⁴²

- addressing the commercial viability issues that are hampering investment in antibiotic development, assessing the relative merits of possible incentives to stimulate research and development in new antibiotics and other products, and fast-track priority review arrangements for new antimicrobials,
- building international partnerships and coalitions to influence change at the national, European and international levels by influencing initiatives like IMI,³³ to facilitate more efficient discovery and development of medicines, vaccines and diagnostics,
- opening up the research agenda, encouraging life sciences companies and academics to work with and share information about targets (pre-competitive phase) and being innovative about the clinical research process to optimise effectiveness and efficiency (shorter time, less costly and fewer late-stage failures) whilst providing safety safeguards.

Key area 5: better access to and use of surveillance data

Actions needed to strengthen surveillance in the human and animal sector are:

- linking clinical and laboratory data in human health to improve control of the most resistant bacteria and to identify key 'drug-bug' combinations detailed at Annex C,
- developing antimicrobial usage and resistance surveillance programmes that can link to electronic prescribing systems as they are introduced,
- improving the quality and standardisation of routine antibiotic testing and interpretation of results as well as making better use of surveillance data to improve diagnosis and treatment of infections,
- exploring linkage of human and veterinary data and consideration of sharing laboratory/ testing methods between the sectors,
- extending alerts about new and emerging antibiotic resistance issues, to a wide range of professionals.

Key area 6: better identification and prioritisation of AMR research needs

Actions to support the better identification and prioritisation of AMR research needs are:

- ensuring funding of high-quality and relevant AMR projects in response to the NIHR themed call announced as part of a co-ordinated response to the publication of the 'CMO's Annual Report'.² This call covers all aspects of translational, clinical and public health research that could contribute to a reduction in the spread or occurrence of AMR, through new developments or changes in practice,
- the NIHR plans to fund a 'Health Protection Research Unit on AMR/HCAI' from April 2014. An open competition inviting universities in partnership with PHE is already underway,

- ensuring that research funders continue to collaborate so that both research needs continue to be identified as the evidence base evolves and key priorities continue to be funded,
- identifying, through expert advice from the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) and the Defra Antimicrobial Resistance Co-ordination Group (DARC), emerging AMR research needs in humans and animals,
- forging stronger partnership around investigating the mechanisms leading to AMR with a view to identify potential new targets for drugs and vaccines.

Key area 7: strengthened international collaboration

Actions needed to strengthen international collaboration with international bodies to improve knowledge and understanding of AMR, improve conservation and stewardship of existing antibiotics and facilitate development of new antibiotics, diagnostics and novel therapies are:

- continuing to demonstrate leadership in the task of building political support for action at a global and national level,
- supporting efforts to strengthen international partnerships and coalitions to facilitate the development of new antibiotics and other treatments,
- seeking assurances from WHO of its commitment to accelerate the pace of progress with respect to implementation of the 2011 WHO 'Global Strategy on the Containment of AMR',⁷
- pressing the European Commission to accelerate progress to implement the '2011 EU AMR Strategic Action Plan',³
- facilitating international action by helping WHO develop a framework for action to underpin an integrated programme of work to harness greater collaborative working,
- taking a leading role in the development of a new AMR resolution for consideration by the World Health Assembly and pursuing supporting action in FAO and OIE (the UN bodies for food and animal health),
- consider the need for a future international treaty to protect special medicines like antibiotics which are in short supply.

Monitoring Trends in Resistance

Changes in the level of resistance to antibiotics like the carbapenems, which are often the last option for hard to treat infections, will be monitored. Generally, the trends will be established by looking at changes in a number of these combinations rather than single combinations.

The following drug-bug combinations are the suggested areas for monitoring in the UK (for humans), to be confirmed by the HLSG.

Multi-Drug Resistant Bacteria	Metric
<i>Klebsiella</i> spp - carbapenem	% non-susceptible to imipenem and/or meropenem
<i>E. coli</i> - carbapenem	% non-susceptible to imipenem and/or meropenem
<i>E. coli</i> - cephalosporin	% non-susceptible to cefotaxime and/or ceftazidime
<i>E. coli</i> – fluoroquinolone	% non-susceptible to ciprofloxacin
<i>Pseudomonas</i> - carbapenem	% non-susceptible to imipenem and/or meropenem
<i>N. gonorrhoeae</i> – ceftriaxone	% non-susceptible
<i>Klebsiella</i> spp - cephalosporin	% non-susceptible to cefotaxime and/or ceftazidime
<i>Pseudomonas</i> – cephalosporin	% non-susceptible to ceftazidime
<i>E. coli</i> – gentamicin	% non-susceptible
<i>S. pneumoniae</i> – penicillin	% non-susceptible

Glossary

Anthelmintics	An agent that destroys or causes the expulsion of parasitic intestinal worms.
Antimicrobial	An antimicrobial is a drug that selectively destroys or inhibits the growth of microorganisms. Sometimes referred to as an 'antimicrobial agent'. Examples include antibiotics (also known as antibacterials) antiviral and antifungal agents.
Antimicrobial resistance (AMR)	The ability of a microorganism to grow or survive in the presence of an antimicrobial at a concentration that is usually sufficient to inhibit or kill microorganisms of the same species and that exceeds concentrations achievable in the human / animal / patient.
Antimicrobial stewardship	The use of co-ordinated interventions to improve and measure the use of antimicrobials by promoting optimal drug regimen, dose, duration and route. The aim is for optimal clinical outcome and to limit selection of resistant strains. This is a key component of a multi-faceted approach to preventing antimicrobial resistance.
Broad-spectrum antibiotics	These are effective against a wide range of bacteria. For example, meropenem is a broad-spectrum antibacterial.
Carbapenems	Carbapenems are broad-spectrum antibiotics, often used as the last line of treatment for hard to treat human infections caused by Gram-negative bacteria.
Carbapenemases	These are enzymes produced by bacteria that destroy carbapenems and other beta-lactam antibiotics.
Cephalosporins	Types of broad-spectrum antibiotics.
Cephalosporins – third-generation	Cephalosporins like cefotaxime and cefixime are particularly active against Gram-negative bacteria.
Critically Important Antimicrobials (CIAs)	Antibiotics identified by the World Health Organisation as critically important for human health and their use needs to be restricted, especially in the veterinary sector.
Disease burden	This includes the economic costs like treatment costs for hospital admissions and the cost to health in terms of mortality and morbidity.
ESBLs	Extended-Spectrum Beta-Lactamases (ESBL) are enzymes produced by bacteria making them resistant to penicillins and cephalosporins.
Gram-negative bacteria	Those bacteria that do not retain crystal violet dye in the Gram-staining procedure. They can cause many types of infection and include <i>E. coli</i> and <i>Pseudomonas aeruginosa</i> .
Gram-positive bacteria	These are bacteria that are stained dark blue or violet in the Gram-staining procedure. They include <i>Staphylococcus aureus</i> and <i>Clostridium difficile</i> .
Healthcare Associated Infections (HCAI)	Infections acquired via the provision of healthcare in either a hospital or community setting.
Macrolides	Type of antibiotics eg erythromycin.
MDR	Multi-drug resistant – resistant to multiple classes of antimicrobial.
Meticillin-resistant <i>Staphylococcus aureus</i>	MRSA - A strain of <i>Staphylococcus aureus</i> that is resistant to beta lactam antibiotics which include penicillins (eg meticillin and oxacillin) and almost all cephalosporin antibiotics.
'One-Health' approach	Collaborative multi-disciplinary work at local, national, and global levels to attain optimal health for people, animals and the environment.
Prevalence	A snapshot at a particular point in time of the total number of cases, or proportion of resistant cases, in a given population.
Primary care	Services provided by GP practices, dental practices, community pharmacies and high street optometrists.
Quinolones	A family of antibiotics, includes broad-spectrum agents like ciprofloxacin.
Responsible prescribing	The use of antimicrobials in the most appropriate way for the treatment or prevention of infectious disease.
Secondary care	Covers acute healthcare, either elective care (planned specialist medical care or surgery, usually following referral) or emergency care.
Zoonosis	A disease that normally exists in animals but that can spread to humans. Examples include brucellosis and lyme disease.

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