HM Government

Government response to the Review on Antimicrobial Resistance

September 2016

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Foreword

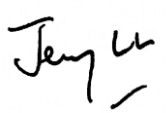
The discovery of penicillin in 1928 was a huge breakthrough for human health, leading to a golden age of antibiotics which saved countless people from infections which previously would have proved fatal. But Sir Alexander Fleming himself warned in his Nobel Prize acceptance speech about the risk of microorganisms developing resistance to penicillin.

In recent decades resistance has become a reality globally. At the same time, there has been a gradual disinvestment in research and development of new antibiotics. There have been no new classes of antibiotics brought into clinical practice since 1987. There is a real risk that, if we do nothing, modern medicine as we know it will be undermined. The loss of reliable antibiotics will mean that straightforward procedures from chemotherapy to hip replacements will become increasingly dangerous. This is a huge health problem in the making and a lack of access to antibiotics means that people are already dying. But it is also a threat to societies and economies around the world, as infections become increasingly untreatable. That is why Lord O'Neill of Gatley was asked to conduct an independent Review into antimicrobial resistance (AMR). Jim O'Neill is a distinguished economist and has brought not only the skills and analysis of an economist to the problem of drug resistance, but also his understanding of emerging economies. He has identified the huge scale of the challenge, but also the concrete steps we can and must take.

The UK Government is determined to meet that challenge. We are already investing £265m through the Fleming Fund for improving laboratory capacity and international surveillance systems and we are using a further £50million to kick start a global AMR innovation fund. Furthermore, we are funding the development of ground-breaking diagnostic tools and will explore how we can make full use of diagnostics to drive appropriate prescribing in the NHS. As promised in our Manifesto, we will lead on implementation of the recommendations Lord O'Neill has made. In particular, we strongly support the Review's recommendation to use global financing systems to reinvigorate both early-stage research, and development of new drugs. We will work through the United Nations and other international fora to support action on AMR.

At home we will continue to drive forward our UK AMR Strategy, setting new ambitions to reduce infections and prescribing, both for animals and humans, recognising they are fundamentally linked.

The threat of drug resistance is very real and it is in all of our interests to tackle it. We are deeply grateful to Jim O'Neill and his team for their hard work. It is now for all of us to do our bit to implement his report.



Rt. Hon Jeremy Hunt MP
Secretary of State for Health

Rt. Hon Andrea Leadsom MP
Secretary of State for Environment, Food and Rural Affairs

1 Introduction

1.1 Last year in their Manifesto the Government committed to continue to lead the global fight against antimicrobial resistance (AMR), taking forward the recommendations of the Review. The UK Government fully intends to fulfil that commitment. We warmly welcome the Review's final report and are determined to lead its implementation.

1.2 The Review is of course a report addressed to the whole global community. No one country can implement it on its own. So whilst we will continue to drive forward our UK AMR Strategy at home we will do all we can to support other countries to develop and implement their own strategies, in line with the World Health Organisation's Global Action Plan on AMR, and agree and share global commitments.

1.3 A global approach includes working closely with Europe. On 23 June, the EU referendum took place and the people of the United Kingdom voted to leave the European Union. Until exit negotiations are concluded, the UK remains a full member of the European Union and all the rights and obligations of EU membership remain in force. During this period the Government will continue to negotiate, implement and apply EU legislation. The outcome of these negotiations will determine what arrangements apply in relation to EU legislation in future once the UK has left the EU.

1.4 We set out below our key commitments in response to the Review, as well as setting out in the Annex to this document our position on each of the Review's recommendations.

1.5 Our top priority is our commitment to working with our international partners to create a global approach to funding new antimicrobials, especially antibiotics. That is our long-term goal to address the market failure we observe at present. But we cannot wait until such a system is in place. We need to take action now to reduce the number of infections, to use the drugs we have better and to ensure appropriate access. We also need to promote research into new drugs, vaccines and therapies. In other words we will aim to prevent infections; protect the drugs we have; and do all we can to promote the drugs pipeline and the development of rapid diagnostics, and knowledge on tackling drug resistance, including surveillance.

1.6 Underpinning all that we do are our increased efforts to enhance surveillance to enable better prescribing, improve our identification of research needs and collaboration, promote understanding and awareness of AMR, and strengthen international collaboration and coordination.

2. The long term goal: A reinvigorated antibiotic pipeline and established systems to protect these lifesaving drugs; increasing supply and reducing inappropriate demand.

2.1 The Government agrees with the Review's analysis that there is an urgent need to both invest in early stage research and the use of diagnostics and stimulate development of new antimicrobial drugs.

2.2 The Government strongly supports the Review's recommendation to use a global system of market entry rewards to reinvigorate the antibiotic development pipeline and address the market failure which has led to an under-investment in antimicrobial products. The aim is to shift incentives for pharmaceutical companies and others to create a sustainable and long-term solution with new rewards, funded globally, that encourage the development of new antibiotics and other antimicrobial products and ensure access to the new antibiotics in the developing world.

2.3 The Government will work to develop global support for these proposals, building on the commitments already made by the G7 and G20 on AMR. The Government will explore with the G20 and wider international community the key principles for financing focusing on how market entry rewards could be financed in the medium term, including through the use of private funding. The report suggests a number of different options and the Government will take these forward to be considered in collaboration with international partners.

2.4 The UK has committed £50m over the next 5 years to set-up a Global AMR Innovation Fund to target and coordinate investment globally. The aim is that this funding for R&D will boost further investments from international governments, third sector, and the private sector. We discuss this further below.

2.5 We are focussing on the development of new antibiotics initially where the research is most lacking, although we recognise that action to tackle antimicrobial resistance needs to address resistance to antivirals, antiparasitics, and antifungals as well as antibiotics.

2.6 Alongside this work to encourage new drugs, co-ordinated international action is needed to embed systems which ensure all antimicrobials – current and future - are used appropriately, and made accessible to those who need them most. Critical to the use of appropriate antimicrobials is the use of cost-effective and rapid diagnostics.

3. Our Domestic Response: building on success, going further and faster with a focus on preventing infection, and reducing inappropriate use of antibiotics in both human and animal health.

3.1 The Review has given renewed impetus to the Government's commitment to tackle AMR in the UK. The UK Five Year Antimicrobial Resistance Strategy published in September 2013, represents an ambitious programme to slow the development and spread of AMR taking a "One-Health" approach spanning people, animals, agriculture and the wider environment. We have made good

progress on implementation and our annual report for 2015 is published today, but we need to go further.

3.2 On prevention, we recognise Lord O'Neill's challenge to strengthen infection prevention and control in both human and animal health. The UK already has ambitious plans for improving infection prevention and control through the UK AMR strategy, but we need to do more**. We will reduce healthcare associated Gram-negative bloodstream infections in England by 50% by 2020.** We will do this by:

- publishing guidance on preventing Gram negative infections;
- publishing locally comparable data on key infections; and
- supporting local teams of NHS England, NHS Improvement and PHE staff to help deliver the ambition, with a special focus on the control of the very concerning emerging carbapenem resistant enterobacteriaceae (CRE) infections, which are now resistant to virtually all antibiotics.

3.3 It is critical that patients receive the antibiotics they need. But to protect those same drugs we must ensure they are only used where appropriate. We have begun to turn the tide on antibiotic prescribing rates for human health with a 7.9% reduction in primary care prescribing in England over the last year, thanks to the excellent efforts of clinicians across the country. But we must go further, faster. **We will reduce inappropriate antibiotic prescribing by 50%, with the aim of being a world leader in reducing prescribing by 2020.**

3.4 Antibiotics are frequently prescribed "just in case" because we lack the diagnostics that could reliably and quickly indicate whether someone has a virus or a bacterial infection. Lord O'Neill has set a major challenge in his Review: not only to revitalise the market to incentivise development of new diagnostics, matching the approach for new drugs, but also to ensure that tests or epidemiological data are used to support clinical decision making.

3.5 We welcome this challenge. We will work with international partners and other relevant groups and funders, such as the research councils, to develop plans for incentivising diagnostic development, and for stimulating the behaviour change needed to realise the benefits for patients.

3.6 In England our vision for diagnostics is to have patient-centred, cost effective diagnostics that help tackle AMR by ensuring the right test is available at the right place at the right time. We have set up an expert group to identify how to achieve that vision and it will work to communicate this health system need to industry, helping them engage with the National Institute for Health Research Office for Clinical Research Infrastructure to ensure the rapid take up of new technologies to **deliver high quality diagnostics** in the NHS.

3.7 It is critical that we focus on stewardship of antibiotics in animals, as well as in humans. The O'Neill Review has advocated country-level livestock antibiotic use targets with a suggested 50mg per kg target. The British meat poultry sector set up an antibiotic monitoring system five years ago and has already demonstrated a 44% reduction in the use of antibiotics, by weight, over the

2012-15 reporting period. Building on this, and taking into account ambitious measures being taken to reduce and optimise antibiotic use in other species sectors too, **the Department for Environment, Food and Rural Affairs (Defra) has committed to a reduction in antibiotic use in livestock and fish farmed for food to a multispecies average of 50mg/kg by 2018 (from the most recent 2014 figure of 62mg/kg) using methodology harmonised across other countries in Europe**. Taking this further, we will work closely with different individual sectors to ensure that **appropriate sector specific reduction targets are agreed by 2017 so that future reductions are greatest where there is most scope,** and that they are underpinned by improvements which focus on encouraging best practice and responsible use of antibiotics and which safeguard animal health and welfare.

3.8 A further crucial element of good stewardship is the restriction of the use of antibiotics which are of highest critical importance to human medicine. Within sector-specific goals on stewardship and reduction of antibiotic use, we will consult with species experts and work with veterinary professional bodies to set agreed rules for such antibiotics so they are reserved as a last resort when there is a disease, with a diagnosis and no alternative treatment, and after conducting an antibiotic susceptibility test. We envisage a significant increase in regulatory oversight of veterinary antibiotics compared with current legislative requirements, enabling restrictions, or even bans, in animals on use of antibiotics of highest priority and critical importance to people, based on scientific recommendations and an evidence based approach.

3.9 The principle of preventing disease holds strong in animal health too. We will continue to work to improve prevention of disease in animal health, focusing on approaches which emphasise improvement in overall biosecurity and overall herd health, including through vaccination (including vaccination in fish farming), in order to improve productivity and maintain competitiveness while reducing the use of antibiotics. One current example in England is the use of Rural Development Programme funding to help farmers in trialling identification, control and eradication of an exemplar endemic animal disease in cattle and pigs, with a view to demonstrating the economic impacts of these diseases and the behaviour changes that can reduce disease risk.

3.10 In addition, the Accelerated Access Review, due to be published later this year, will set out a bold new vision where patients, the NHS, innovators, and clinical leaders work together to pioneer and accelerate evidence-based technologies, including new medical technologies and diagnostics. The proposals in the Accelerated Access Review will set out how the NHS can embrace the transformational technologies it needs to improve efficiency and outcomes, including the use of diagnostics so that medicines are used at the right time.

3.11 To support better stewardship of antibiotics, it is critical we promote greater understanding amongst the public. We ensured that World Antibiotic Awareness Week takes a “One-Health” approach with both human and veterinary health professionals working closely to give a unified message across the UK. We launched our Antibiotic Guardian campaign calling for

action in the form of on-line pledges from both professionals and members of the public across both sectors and have achieved nearly 32,000 pledges of support.

4. We will run a regional, highly targeted pilot campaign to determine the most effective way to raise awareness of antimicrobial resistance, and drive behaviour change amongst key audiences.

4.1 The campaign will support existing national activity aimed at prescribers and other health care professionals by improving understanding of the issue, decreasing demand and increasing acceptance of a decision not to prescribe antibiotics. We will adopt a 'test and learn' approach to determine the most effective driver with each audience, and will use these insights to inform larger scale activity next year.

4.2 However we recognise that Lord O'Neill calls for a global public awareness campaign and we will work with partners to explore how this might be achieved and champion the recommendation at the UN General Assembly meeting on AMR in September.

4.3 Underpinning all this activity is good surveillance. The UK has world-leading surveillance systems. For the first time in 2015 we published a One-Health surveillance report encompassing antibiotic resistance and consumption data across human and animal sectors[1]. We will build on this record and enhance our One Health surveillance systems further.

4.4 On environmental discharges, we will continue to participate in the Europe-wide programme to monitor substances of concern in the water environment and completing our assessment of the presence of antibiotics in the effluent from waste water treatment plants across the UK. We will use the developing evidence base to inform any future regulatory action on such discharges to the environment. We will also work with the UN Environmental Programme to see how standards in this area might be raised globally.

4.5 Current regulations place requirements on manufacturers of antibiotics to limit the emission of specific substances that may cause harm to human health and the environment. We will encourage the pharmaceutical industry in the UK to maintain their proactivity in the area of developing a better understanding of the environmental transport, behaviour, fate and effects of pharmaceuticals, and to be mindful of these issues where ever the antibiotics active ingredients are produced.

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1 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/477962/ESPAUR_Report_2015.pdf

5. Working internationally: achieving long-term goals through globally co-ordinated and sustainably funded action

5.1 The Review on AMR rightly takes a global perspective as AMR is a global issue, with resistant microorganisms paying no heed to national boundaries. It can therefore only truly be tackled by collaboration within and between nations.

5.2 Last year saw major progress in international commitments to action to tackle AMR, in particular with agreement to an AMR Global Action Plan (GAP) in the WHO, with equivalent resolutions at the Food and Agriculture Organisation of the UN (FAO) and the World Organisation for Animal Health (OIE). These commitments provide a strong blueprint for the world, covering the range of actions required to tackle this major global challenge and we welcome the consensus that the GAP has attracted.

5.3 We will build on this in 2016. The Review provides further evidence of the urgency of the issue. The recommendations give us a good basis for giving political impetus to the implementation of the AMR Global Action Plan, working with our international partners.

5.4 The Global Foreign Policy Resolution made by the United Nations, in December 2015, called for a High Level Meeting at the UN General Assembly in September 2016. We are working hard with partners to ensure that this meeting will bring the high level political attention to AMR needed to ensure action is taken across all sectors. We believe the Review recommendations make a valuable contribution to the debate in the run up to this meeting.

5.5 We will seek to use the high level political declaration that will be negotiated for this meeting to garner international support to take forward work in the areas set out in both the GAP and now in the Review's final report.

5.6 In particular we are working with lower and middle income countries (LMICs), recognising that AMR risks undoing decades of development progress globally by limiting our ability to control infection and keep routine medical procedures safe. Health systems in LMICs will be hardest hit when resistance develops to first and second line drugs. Such resistance threatens to undermine progress towards all the Sustainable Development Goals (SDGs), especially SDG3 on health[2].

5.7 On animal health, we will continue to support OIE initiatives to progress action on AMR, including contributing technical expertise on surveillance and identification of vaccines that have a high impact on reducing antibiotic use in animals.

5.8 For this reason we will be looking to engage broadly with international counterparts globally, particularly those in LMICs to support them to take

[2] http://www.reactgroup.org/news/524/18.html

national action to tackle AMR in line with the Review recommendations. We want to ensure action to tackle AMR is integrated with broader health development priorities, including strengthening implementation of the International Health Regulations, and that international action on AMR reflects the circumstances and needs in developing countries as well as the developed world.

5.9 We are acutely aware that we need to work closely with developing countries to improve access to appropriate drugs for patients, including both existing antimicrobials and new products, as they are developed. In December 2015 the former Chancellor launched the Ross Fund which aims to develop, test and deliver a range of new products (including vaccines, drugs and diagnostics) to help combat the world's most serious diseases specifically in developing countries. A key part of the Ross Fund, which is cumulatively worth £1bn, is the £265m Fleming Fund to improve surveillance and enhance laboratory capacity and diagnosis, as well as data and surveillance of AMR in people and animals.

5.10 Within the Ross Fund, the UK has also committed £50m over 5 years to set-up the Global AMR Innovation Fund. This aims to coordinate and target investment globally in neglected and underinvested areas and to stimulate investment in AMR R&D globally. Following the Review recommendations, we are currently working in collaboration with China and other organisations, such as the Bill and Melinda Gates Foundation, and engaging internationally with other governments, third-sector, and industry to leverage the additional $2bn USD of global investment required for AMR R&D.

5.11 Since 2015, the Newton Fund has committed £6.5 million specifically on antibacterial resistance research. Through the Medical Research Council (MRC) over £2m was committed with matched funding from India to support two joint UK- India centres focussing on new diagnostic tools and treatments to address multidrug resistant tuberculosis and developing smart materials for the detection and targeted delivery of antibiotics for eye infections to prevent inappropriate use of antibiotics. In addition, since the announcement of a UK-China partnership during the October China State visit, the MRC, the Biotechnology and Biological Sciences Research Council (BBSRC), and the Economic and Social Research Council (ESRC) committed £4.5 million with matched funding from China to support 6 large research projects on AMR.

5.12 Access to clean water is crucial for infection prevention and control but is still a luxury for far too many. We are committed to help 60 million people gain access to water and sanitation by 2020 to stop terrible diseases. We are on-track to meet this target through a range of country and central programmes funded by the Department for International Development (DFID). We continue to be one of the largest funders of research into water and sanitation to find more effective ways to deliver services more cheaply and quickly.

6. Conclusion

6.1 Tackling drug resistance is one of the most critical challenges we face. It will not be solved by one country acting alone, but by the global community working together to deliver the WHO's Global Action Plan on AMR. The UK Government remains determined to be at the forefront of support for delivery of that plan.

6.2 The final report of the Review on AMR has mapped out the major global challenge of increasing drug resistance and set out a clear direction to follow. This initial, high level response to the Report will be followed with a more detailed implementation plan, which will reflect what is agreed at the UN General Assembly meeting on AMR in September this year. We will integrate our commitments into our UK Strategy, and continue to report progress on that annually.

Summary list of recommendations

This represents a summary of the recommendations contained in the main report. The order in which these are presented reflects the structure of the report and not any kind of suggested prioritisation.

1	*A major global public awareness campaign*	*Lead Dept.*	*Government action/commitment*
1.1	With leadership from an appropriate global body, establish an internationally-coordinated public awareness campaign to improve public understanding of the problems of drug resistance and support positive behaviour change regarding antibiotic use. Whilst globally consistent in its overall message, this should be delivered at country or regional level, with the message and the medium (e.g. social media, broadcast advertising, and celebrity endorsement) tailored to local and regional norms.	DH/FCO	• We will work to encourage the international adoption of this recommendation through the UNGA High Level Meeting and will work with partners to see how this could be operationalised.
		PHE	• We will begin piloting a public-facing awareness campaign in England through PHE to address antimicrobial resistance in 2016/17 and will evaluate its effectiveness.
		MHRA	• MHRA have launched the Fake Meds campaign targeting the public that aims to change behaviour in online purchasing and direct consumers towards safe online medical product purchase. The campaign will use a variety of communications channels and partnerships to promote messaging focused medicines and devices that are frequently falsified.
1.2	At a country level, establish robust regulations to prevent the sale of antibiotics and other antimicrobials 'over-the-counter'	MHRA/VMD	• MHRA will continue to monitor the safety and efficacy of these products wherever they are advertised, sold or supplied, including through the

	(OTC) without a prescription, and ensure that these are properly enforced. Such policies to be locally-tailored to recognise instances where OTC sales may be only means of accessing antimicrobials – but where this is the case, provision of proper, clinician-led access should be a priority.		internet. MHRA will continue to keep systemic antibiotics as Prescription Only Medicines (POM) and take additional appropriate regulatory action where necessary. • The VMD will continue to keep all antibiotics as prescription only veterinary medicines, which may only be prescribed by a vet (POM-V) and take appropriate regulatory action where necessary. • The VMD will continue to work closely with a range of enforcement partners to tackle the illegal sale of antibiotics. Regular dialogue with UK Border Force has brought success, as has VMD's close working relationship with internet sales platforms and cross-border collaborations with our European colleagues. • We will continue to work with the WHO and its partners to support the development of a Global Stewardship Framework and ensure it is takes into consideration different models of Stewardship needed in LMICs with limited health infrastructure.
1.3	Global organisations (including the WHO, INTERPOL and World Customs Organization) to ensure a robust and internationally-coordinated effort to prevent cross-border sales of antimicrobials over the internet without prescription. This should be supported by outright bans on non-prescription internet sales at country level.	MHRA	• MHRA will continue to work with global organisations on this agenda. For example in 2015 MHRA participated in the 'Operation Pangea VIII' initiative, coordinated through INTERPOL to seize counterfeit and unlicensed medicines and devices. • MHRA have developed a campaign targeting the public that aims to change behaviour in online purchasing and direct consumers towards safe online medical product purchase. • MHRA continues to operate the Common Logo scheme, where online retailers of medicine are mandated to display a logo on their e-commerce web-pages to show they are an authorised

			retailer. Consumers in turn are encouraged to use the logo to confirm retailer authorisation. This scheme, introduced in June 2015 through the Falsified Medicines Directive, complements the existing work of MHRA to tackle the illegitimate online sale of medicines.
		VMD	• The VMD operates a similar, voluntary scheme for veterinary medicines – the Accredited Internet Retailer Scheme – and will continue to take actions against illegal online advertising and sales.
2	***Improve sanitation and prevent the spread of infection***		
2.1	Governments, insurers, regulators and other healthcare system leaders should embed infection prevention and control (IPC) as a top priority at all levels within healthcare systems, using defined healthcare-associated infection (HCAI) reduction goals as the basis for targets, incentives and other performance management measures.	DH/PHE, NHS Improvement and NHS England	• Specific additional work is underway to support the delivery of a reduction in healthcare associated Gram-negative bacteria infections in England by 50% by 2020. • Infection prevention and control is a key part of the UK AMR Strategy's prevent pillar, with a wide ranging programme that includes: • using commissioning and regulatory structures e.g. CQUINs to reduce healthcare associated infections and improve prescribing; • work by PHE regions and centres to support organisations achieve their local infection reduction targets; • work to ensure that infection prevention and control is a key focus within the Care Quality Commission's inspections; • work to develop local leadership on AMR, including PHE and NHS England and NHS Improvement to

			help support its delivery.
2.2	Public and philanthropic funding bodies to support modest improvements in funding for studies that demonstrate the effectiveness and cost-effectiveness of novel IPC interventions in health and care settings, and measures to induce positive behaviour change by clinicians and other healthcare workers.	DH	• DH will continue to work with public and philanthropic funding bodies and through NIHR Heath Protection Research Units to develop research proposals and highlight the areas that require investigation (with NIHR, Wellcome Trust, professional societies, EU, Research Councils). The research on AMR will include both human and animal health sectors. • We collaborate closely with other countries on the AMR action package under the Global Health Security Agenda (GHSA) initiative to share best practice and call for reference to the importance of IPC in the UN declaration on AMR. • DFID continues to invest in health system strengthening to improve service delivery, which in some cases includes building capacity on IPC.
2.3	Governments of low- and middle-income countries should ensure that the benefits of improved public health and reduced antimicrobial resistance are properly factored into investment decisions about improved access to water and sanitation infrastructure.	DFID	• UK Government (through DFID) has committed to help 60 million people to gain access to water and sanitation by 2020 to stop terrible diseases. We are on-track to meet this target though a range of country and central programmes. • We continue to be one of the largest funders of research into water and sanitation to find more effective ways to deliver services more quickly and cheaply. • We will support the implementation of the WHO GAP on AMR in low and middle income countries where IPC is a key pillar of their NAPS.
3	***Reduce the unnecessary use of antimicrobials in agriculture and their dissemination into the environment***		

3.1	The G20 and UN, with input from the WHO, FAO and OIE, should lead urgent global efforts to improve the collection and use of surveillance data regarding the use of antibiotics in agriculture, and the emergence and spread of drug-resistant strains of microbes amongst animals. This should be prioritised over the next two years to inform targets to reduce unnecessary use of antibiotics starting in 2018.	Defra	• We will encourage the international endorsement of improved surveillance systems through the UNGA High Level Meeting to enable countries to work towards setting targets appropriate to their national context. • The OIE has a strong pre-existing workstream in this area and we will support their initiatives wherever possible. • We will use Fleming Fund to support FAO and OIE in their efforts to improve the collection of surveillance data regarding the use of antibiotics in agriculture and the occurrence of drug-resistant bacteria in animals. • We will work to encourage the international endorsement of this recommendation through the UNGA High Level meeting. • Defra and VMD will ensure that infection prevention and control is a principal part of good animal husbandry practices
		FSA/Defra	• Codex Alimentarius (the joint FAO/WHO body dealing with food) has agreed to establish an intergovernmental task force on antimicrobial resistance in 2017, the terms of reference for which will be developed by a working group that the UK will host later this year and will co-chair with the USA and Australia..
		FCO	• Engagement through the UK's diplomatic network to generate support for an ambitious outcome at the UN High Level Meeting.
3.2	International institutions with the relevant experience should undertake now a detailed	Defra/FCO/ DFID	• We will work to encourage the international endorsement of this recommendation through the UNGA High Level Meeting and welcome efforts by

	economic analysis of the transition costs associated with lowering the use of antibiotics in farming across different regions and countries – particularly those in low and middle-income settings, where less analysis has been done to date		the World Bank to bring forward proposals that may contribute to this.
		FCO/DFID	• We welcome the commitments made and economic analysis provided by international organisations to date, including the World Bank and the OECD, to make progress on this agenda and we commit to work with all parties to develop both AMR-sensitive and AMR-specific activities.
3.3	The WHO, FAO and OIE should, as a matter of urgency, convene a global group of experts, working across the relevant regulatory bodies and international organisations, to agree a single, harmonised list of those antibiotics most critical to human health. This would help to inform those antibiotics that should be banned or restricted from use in agriculture.	Defra/DH	• We will continue to support development of veterinary legislation which enables restrictions or even bans on use in animals of antibiotics which are of highest priority and critical importance to people, based on scientific recommendations and following evidence based approach.
		FCO	• We will work to encourage the international endorsement, through the UK's diplomatic network, of this recommendation through the UNGA High Level Meeting and ensure relevant agencies are involved in any follow up work.
3.4	Food producers and retailers to take steps to improve transparency for consumers regarding the use of antibiotics in the meat that we eat, to enabling better informed decision-making by customers. As part of this we call on major producers, retailers and regulators to agree standards for 'responsible use', to be used as the basis for an	Defra/FSA	• We believe that consumers are able to engage with complex issues relating to their interests in relation to food if they are given the right support and opportunities to do so. We also believe that providing greater transparency on business standards will incentivise rapid and comprehensive improvement, support innovation and reward responsible businesses.

	internationally recognised label, or used by existing certification bodies.		• We will therefore encourage food manufacturers, assurance scheme and retailers to: • develop standards for the responsible use of antibiotics in poultry, pig and dairy sectors and incorporate these into standards for consumer-facing assurance scheme standards; • set clear expectations about the information on usage of antibiotics that industry should publish as open data, and • work with consumers to understand and articulate the issues that matter to them so that we and other interested parties can develop new tools and applications using open data that support consumers in taking greater responsibility for the food decisions they make and their impacts. • The UK, together with Australia and USA, will be hosting a working group later this year with the aim of establishing the terms of reference for the international task force which, if agreed by the Codex Alimentarius Commission in summer 2017, will work on a range of food safety issues including international assurance and labelling schemes.
		FCO	• Engagement through the UK's diplomatic network to generate support for an ambitious outcome at the UN High Level Meeting.
3.5	In 2018, defined targets should be established at the country level to reduce unnecessary use of antibiotics in agriculture. There will not be a one-size-fits-all target, but all countries need to play their part in	Defra	• We will reduce antibiotic use in livestock and fish farmed for food to a multispecies average of 50mg/kg by 2018 (from the most recent 2014 figure of 62mg/kg) using methodology harmonised across Europe. • Taking this further, we will work closely with

	reducing use. An international panel of experts will be needed to guide the design of these targets and help countries implement them, alongside support from the WHO, FAO and OIE. Our suggestions on how they could be formulated: targets could be set over 10 years, with milestones to ensure regular progress, for reductions in total agricultural usage of antibiotics. These could be defined on the basis of milligrams of antibiotic used per kilogram of meat or fish production, with consideration given to appropriate variation by species. 50 mg/kg would be a reasonable objective for many high-income countries, but each country will need to have and regularly review their own ambitious targets.		individual sectors to ensure that appropriate sector specific reduction targets are agreed by 2017 so that the future reductions are greatest where there is most scope, and that they are underpinned by improvements in animal husbandry, stockmanship, biosecurity practices and disease prevention measures including through vaccine use, and that animal health and welfare are safeguarded. • Within sector specific strategies, we will consult with species experts to set agreed rules for antibiotics, which are most critically important for human health, and which reserve them as a last resort, when there is a disease, with a diagnosis and no alternative treatment, and after conducting an antibiotic susceptibility test. • Internationally, we will continue to play a leading role with international bodies working to improve regulated access and responsible use of veterinary antibiotics globally, taking a staged approach to support capability, infrastructure and improved surveillance. In this way, including through the UNGA process, we will advocate for countries to work towards setting targets in a way which is appropriate for each country and region.
3.6	Global bodies/national governments and regulators should establish evidence-based, enforceable targets for maximum levels of antimicrobial active pharmaceutical ingredient (API) discharge associated with the manufacture of pharmaceutical products.	Defra	• We will use the developing evidence base to help inform any future regulatory action on discharges to the environment. • We will support and steer research into the flow of antibiotic resistance genes, antibiotics and pathogens in the environment and the efficiency of different treatment methods such as anaerobic digestion, wastewater treatment and sustainable

			drainage systems. • We will work to engage environmental ministries and agencies, from around the globe, in AMR through the UNGA High Level Meeting. A global approach includes working closely with Europe. We are currently participating in the EU-wide programme to monitor emerging substances of concern in the water environment. • We will work with the European Commission and Member States over the next two years to consider whether additional antibiotic substances should be classed as Priority Substances at the next review of the relevant EU law. We will complete the assessment by 2020 (as part of the Chemicals Investigation Programme) of the presence of antibiotics in the effluent from waste water treatment plants across the UK. •
		FCO	• International engagement through the UK's diplomatic network to generate support for an ambitious outcome at the UN High Level Meeting.
3.7	Pharmaceutical companies should improve monitoring of API emissions from directly-operated manufacturing facilities as well as those of third party suppliers, and support the installation of proper waste processing facilities to reduce or eliminate API discharge. Such efforts should be based in voluntary, transparent and auditable commitments, with a globally-consistent 'quality mark' applied to end products produced on 'environmentally	Defra	• We will encourage the pharmaceutical industry in the UK to ensure a good understanding of the environmental transport, behaviour, fate and effects of pharmaceuticals, and to take action to limit environmental contamination wherever they manufacture antimicrobials, or their active ingredients. • As part of broader awareness raising we will raise awareness of the issue of antimicrobial resistance and the environment.

	responsible' basis.		
4	***Improve global surveillance of drug resistance and antimicrobial consumption in humans and animals***		
4.1	WHO to provide global leadership and coordination to efforts – supported from governments, regional organisations, and philanthropic organisations – to establish a global surveillance system to monitor the emergence and spread of drug-resistant infections.	DH	• We will commit £265m over 5 years (the Fleming Fund) to improve "one health" laboratory capacity and surveillance systems in low and middle income countries, working closely with WHO, FAO and OIE.
4.2	National governments/regulators and globally-representative bodies to initiate work to incentivise and remove barriers to the safe, secure and appropriate sharing of data of use to global surveillance efforts between public and private organisations on a large scale, with a particular view to unleashing the potential of advances in 'big data', cloud computing and machine learning in the coming years.	DH PHE	• We will continue to work across the health sector to ensure that organisations that hold patient level data develop data safe havens. This will include appropriate governance structures to develop big data approaches, including machine learning and Bayesian methodologies that will improve our understanding of infection transmission, intervention and control dynamics. • We will continue to work with the WHO to encourage the adoption of the Global Antimicrobial Resistance Surveillance System (GLASS) which endorses common protocol for data collection and the international sharing of said data. • We will use the Fleming Fund investments to encourage the international sharing of data from all sources.
5	***Support the innovation and uptake of rapid point-of-care diagnostics***		

5.1	In high-income countries, governments, regulators and other health system leaders to implement systems of direct incentives to support the uptake and use of rapid point-of-care diagnostics in primary and secondary care. Incentives should be supported in high-income countries by the mandatory use of such tests to support clinical decision-making, where they are available, or the use of up-to-date epidemiological data where they are not, by 2020.	BEIS/NESTA and Innovate UK	• The Longitude Prize was launched in November 2014 with a prize fund of £10M and is a five-year challenge to develop a new diagnostic test for bacterial infections that is accurate, rapid, affordable and easy-to-use anywhere in the world. The Discovery Awards were launched in May 2016 to help teams progress their ideas for the Longitude Prize through seed funding to develop their ideas for a transformative diagnostic test to win the Longitude Prize.
		DH/PHE/NHS England/ NICE/NHS Improvement/ OLS	• The Government is already working to promote point of care diagnostics as a key project in the UK AMR implementation plan, but recognises that a step change is necessary to accelerate this work. We will therefore work with relevant bodies, including PHE, NHS Improvement, NHS England and the National Institute for Health and Care Excellence (NICE), in 2016/17 to explore the feasibility of assessing the effectiveness of existing diagnostics. • The Accelerated Access Review, due for publication later this year will set out proposals for how the NHS can embrace the technologies it needs to improve efficiency and outcomes, including the use of cost effective diagnostics so that medicines are used at the right time.
		NHS England	• NHS England has launched a new programme to fast-track cutting-edge innovations from across the globe to the NHS frontline by providing an explicit national reimbursement route for new medical technology innovations.

			• The programme includes a new Innovation and Technology tariff category which will remove the need for multiple local price negotiations, and instead guarantee automatic reimbursement when an approved innovation is used, while at the same time allowing NHS England to negotiate national 'bulk buy' price discounts on behalf of hospitals, GPs and patients.
5.2	In low and middle-income countries, the uptake and use of rapid point-of-care diagnostics to guide the use of antimicrobials should be supported via a globally administered 'diagnostic market stimulus' system, providing a direct per unit subsidy to diagnostic test manufacturers upon evidence of their product's purchase or use.	DFID	• This recommendation will be considered as part of our overall consideration of how to create a sustainable funding system for AMR. • DFID is providing funding to the Foundation for Innovative New Diagnostics (FIND), a product development partnership which has launched a new programme looking at acute febrile illness and anti-microbial resistance, following completion of a landscape analysis in this area. Their products in development include tests to differentiate bacterial from non-bacterial fever and malaria.
6.	***Improve the use of existing vaccines, and promote the development of new ones***		
6.1	Promote the uptake and use of existing vaccines more widely in humans and animals to save lives and reduce unnecessary antibiotic use, including through the work of Gavi or by initiating comparable new initiatives.	DFID, Defra	• The UK is the largest donor to Gavi, the Vaccine Alliance, providing £1.44bn for 2016-2020 (26% of Gavi's funding). The UK commitment will immunise an additional 76m children against vaccine preventable diseases and save 1.4m lives. • The UK also supports WHO's Global Polio Eradication Initiative, providing £300m for 2013-2019. The UK supports immunisation results at country-level through bilateral support for health systems strengthening.

			• We are supporting a number of programmes on TB in several high burden countries: • DFID is working alongside other donors, supporting several public-private product development partnerships (PDPs), to develop new drugs, vaccines and diagnostics for TB: ➢ the Reduction of TB in Mining Communities of Southern Africa; ➢ the PATHS2 project in Nigeria, which supports a combination of interventions involving the training of community health extension workers and laboratory technicians, establishment of TB Directly Observed Therapy (DOT) Centres, and the supply of basic laboratory equipment and consumables to rural health facilities in Nigeria; ➢ In Burma, the UK supports the 3MDG Fund – some of funds for this programme will be for TB activities, which will contribute to improvement active case finding for TB in populations at high risk such as prisons, mines and urban slums, and diagnosis and treatment for multi-drug resistant TB patients. • We will continue to contribute expertise to OIE activity identifying research gaps for development of new animal and fish vaccines. • Nationally, we will continue to engage with UK livestock sectors and the veterinary pharmaceutical industry to explore further where vaccines can have greatest impact on antibiotic usage.
6.2	Sustain a viable market for vaccines with the greatest potential in tackling drug resistance. Depending on the characteristics of the	HMT/DH	• This recommendation will be considered as part of our work on a global system that rewards companies that develop new, successful antibiotics and other

	vaccines in question, this might be through 'pull' funding using a similar form to existing Advanced Market Commitments (to promote broad uptake in mid to large sized populations), or as market entry rewards (to ensure availability for smaller populations at high risk).		products and make them available to all who need them.
7.	***Closing the skills gap in AMR-related research, and infectious diseases clinical practice***		
7.1	Governments, healthcare system leaders and private actors (such as clinical professional bodies and academic institutions), should work together to expand funding and training opportunities to increase the number and capacity of healthcare workers on the frontline of fighting resistance, and of academic scientists working in the field. These efforts should extend to considering the pay, recognition and standing of professionals working in fields relevant to AMR within the healthcare, academic, and commercial communities.	BEIS/DH	• The AMR Research Funders Forum is conducting a research skills audit in the UK. The first phase of the work, focussed on identifying gaps in skills and capacity for AMR Research in the UK is due to report before end 2016.
		DH	• In England we have strengthened the Health and Social Care Act 2008 Code of Practice on the prevention and control of infection and related guidance. The changes have strengthened infection prevention and control requirements for healthcare providers. • We will ensure that Health Education England will: ➢ build on work started in 2014 to ensure that the antimicrobial stewardship and prescribing competencies developed by the Antimicrobial Resistance and Healthcare Associated Infection advisory committee are embedded in professional curricula, including considering

			the results of the review undertaken in 2015/16; ➢ develop and implement an action plan for promoting examples of good practice by December 2016; ➢ continue cross-system work to develop and promote resources to support antimicrobial stewardship and good infection, prevention and control practices. Action to support the ambition to reduce Gram negatives should be a priority for 2016/17. • Evaluate the impact and uptake of Health Education England's introductory e-learning package on antimicrobial resistance that has a particular focus on infection prevention and control, to assess individual and organisational buy-in and usage by December 2016.

8.	***A global innovation fund to re-invigorate early-stage R&D***		
8.1	Governments and public and philanthropic research funding organisations, to collaborate on a global basis to develop a Global Innovation Fund for R&D into new antimicrobials and other related products (including vaccines and diagnostics.) This fund should build on existing bilateral and multilateral arrangements for pooling and coordinating the spending of research funds, but do more to ensure that AMR-related research is properly funded and more proactively targeted towards neglected areas (e.g. re-purposing of older products.)	DH	• The UK has committed £50m over 5 years to set-up a Global AMR Innovation Fund to target investment globally in neglected and underinvested areas. The aim is that this funding will be boosted through further investments from international governments, third sector, and the private sector, with the goal of leveraging additional investment for AMR R&D globally. The Global AMR Innovation Fund represents an excellent first step towards meeting the need identified by the Review of $2bn additional investment in research over the next five years. The Global AMR Innovation fund is currently collaborating with China and other organisations, such as the Bill and Melinda Gates Foundation and engaging internationally to identify new partners.
9.	***Promote the development of new antibiotics, and make better use of existing ones***		
9.1	Institute a system of 'market entry rewards' to provide lump-sum payments to the successful developers of new antibiotics that meet a specified unmet medical need. In principle, this should be administered and funded on a supranational basis, with support for global, affordable and responsible access to antibiotics at its heart. Detailed work on the design and implementation of such a system picked up as a matter of urgency by the appropriate international partners.	HMT	• We are leading discussions within the global finance and health community, including G20 and G7, to create an innovative and sustainable global system that rewards companies that develop new, successful antibiotics and makes them available to all who need them, and we are committed to finding a successful solution.

9.2	Consider the role that such a system of market entry rewards can play in supporting the development of complete treatment regimens for tuberculosis (TB), as a means of 'supercharging' systems of support for product development.	HMT	• This will be a part of the G20 conversations on market entry rewards.
		DFID	• The Department for International Development is funding the Access to Medicine Foundation. The Access to Medicine Index analyses and ranks the performance of the R&D-based pharmaceutical industry to incentivise increased engagement in improving access to medicines by the poor, which in turn contributes to better health in developing countries. DFID has also discussed with the ATMF the prospect of developing other indexes to measure activities concerning AMR specifically and the impact of these interventions together will lead to an increased influence on the private sector to support product development and take other steps to reduce the rise of resistance.
9.3	Key regulatory agencies should work together to improve the global harmonisation of regulatory pathways for new antibiotics, and explore the possibilities for mutual recognition of regulatory approval across multiple jurisdictions.	MHRA VMD	• MHRA and VMD will continue to discuss with key regulatory agencies in other countries on how to improve regulatory harmonisation on AMR and continue to provide advice and training on establishing regulations. • We will continue to work with Japan as they champion the harmonisation of international regulators through their G7 presidency.
9.4	Pharmaceutical companies, regulators and healthcare system leaders to work together to institute national and regional 'clinical trial networks' for antibiotics, to streamline the	DH/ NIHR	• The NIHR has set up in this country a world-leading Clinical Research Network to deliver high quality research including trials. We note that the independent Review is leading an international working group on clinical trial networks and we look

	clinical trial process and reduce the costs and duration of antibiotic development.		forward to its report with interest.
10.	***Ensuring a globally coordinated and sustainably funded response***		
10.1	The G20 group of countries should take leadership on defined aspects of the global response to AMR, particularly work to develop and implement new incentive models to support the development of new antibiotics, diagnostics and vaccines. This should be complementary to wider discussions on the global response to AMR as part of the UN General Assembly, and the continuing efforts of the WHO, FAO and OIE in their respective sectors.	Cabinet Office, HMT	• We are leading discussions within the global finance and health community to create an innovative and sustainable global system that rewards companies that develop new, successful antibiotics and makes them available to all who need them, and are committed to finding a successful solution. • The UK will champion debate within international fora such as the G20 and the UN on how these rewards could be financed, including through the use of private sector funding.
		FCO	• International engagement through the UK's diplomatic network will generate support for an ambitious outcome in the G20.
10.2 10.3	Governments and relevant global bodies to initiate rapid work to consider in detail the global coordinated structures which would be required to oversee the development, implementation and operation of global systems of financial support for antibiotic and diagnostic development and use. Governments, industry and relevant global bodies should continue to work together to identify adequate and sustainable global, national and local funding mechanisms for	HMT	• The Government welcomes the commitments made by international organisations to date, including the World Bank, to make progress on this agenda and we are committed to delivering solutions working with all parties to develop AMR-sensitive and AMR-specific activities.

	raising the money required to finance a long-term global response to AMR. This should include the exploration of – amongst other options – mechanisms to raise revenue from new sources and on a hypothecated basis, for instance through modest and targeted levies on antibiotic use and/or on the global pharmaceutical, healthcare products, industry and medical devices.		

Glossary

AMRFF	Antimicrobial Resistance Funders Forum
Accelerated Access Review	The Accelerated Access Review aims to speed up access to innovative drugs, devices and diagnostics for NHS patients
Antibiotic	A drug that destroys or inhibits the growth of bacteria. The action of the drug may be selective against certain bacteria.
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.
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.
APIs	Active pharmaceutical ingredients
Bacteraemia	The presence of bacteria in the bloodstream
Beta-lactam antibiotics	β-lactam antibiotics (beta-lactam antibiotics) are a broad class of antibiotics, consisting of all antibiotic agents that contain a β-lactam ring in their molecular structures.
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 which destroy carbapenems and other beta-lactam antibiotics.
Codex Alimentarius	Codex Alimentarius (or "Food Code") - established by FAO and the WHO to develop harmonised international food standards and protect consumer health.
CQUIN	Commissioning for Quality and Innovation (a payment framework allowing commissioners to reward excellence, by linking a proportion of English healthcare providers' income to the achievement of local quality improvement goals)
Critically Important Antimicrobials (CIAs)	Antibiotics identified by the World Health Organisation as critically important for human health.
Defra	Department for Environment, Food and Rural Affairs
DH	Department of Health
DFID	Department for International Development

ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
FAO	Food and Agricultural Organisation of the United Nations
FCO	Foreign and Commonwealth Office
FSA	Food Standards Agency
GAP	Global Action Plan (World Health Organisation provides framework from which all countries can develop and implement their own action plans)
Gavi	Global alliance for vaccines and immunization (Gavi) is a global health partnership working to improve access to immunisation in poor countries.
GHSA	Global Health Security Agenda
GLASS	Global Antimicrobial Resistance Surveillance System - (GLASS) supports a standardised approach to the collection, analysis and sharing of data on antimicrobial resistance at a global level.
Gram-negative bacteria	Those bacteria that do not retain crystal violet dye in the Gram-staining procedure for the preliminary identification of bacteria. These bacteria can cause many types of infection and include *E. coli* and *Pseudomonas aeruginosa*.
Gram-positive bacteria	These are bacteria that are stained dark blue or violet in the Gram-staining procedure. They include *Staphylococcus aureus* and *Clostridium difficile*.
G 20	Group of 20 (Argentina, Australia, Brazil, Canada, China, France, Germany India, Indonesia, Italy, Japan, South Korea, Mexico, Russia, Saudi Arabia, South Africa, Turkey, United Kingdom and United States, plus the European Union)
G7	The Group of seven (Canada, France, Germany, Italy, Japan, United Kingdom and United States)
Healthcare associated infections (HCAI)	Infections acquired via the provision of healthcare in either a hospital or community setting.
HMT	Her Majesty's Treasury
Innovate UK	Innovate UK is the UK's innovation agency and is an executive non-departmental public body, sponsored by the Department for Business, Innovation & Skills.
IPC (Infection Prevention and Control)	Infection prevention and control measures aim to ensure the protection of those who might be vulnerable to acquiring an infection both in the general community and while receiving care due to health problems, in a range of settings. The basic principle of infection prevention and control is hygiene.
LMICs	Low and middle income countries
Market entry rewards	A system of payments to successful developers of new antimicrobial products
MHRA	Medicines & Healthcare products Regulatory Agency
Multi-drug resistant	Resistant to multiple classes of antimicrobial.

Meticillin-resistant *Staphylococcus aureus*	MRSA - A strain of *Staphylococcus aureus* that is resistant to beta lactam antibiotics which include penicillins (e.g. meticillin and oxacillin) and almost all cephalosporin antibiotics.
NAP	National Action Plans on AMR
NESTA	National Endowment for Science, Technology and the Arts - an independent charity that works to increase the innovation capacity of the UK.
NIHR	National Institute for Health Research
OECD	Organisation for Economic Cooperation and Development
OIE	World Organisation for Animal Health (Office International des Epizooties)
OLS	Office of Life Sciences
OTC	"Over the Counter" (reference to sale of antibiotics and other antimicrobials 'over-the-counter')
"One-Health" approach	Collaborative multi-disciplinary work at local, national, and global levels to attain optimal health for people, animals and the environment.
Pathogen	An infectious agent (bug or germ), a microorganism such as a virus, bacterium, or fungus that causes disease in its host.
PATHS2	Partnership for Transforming Health Systems Phase II (PATHS2) is a six-year health systems strengthening project in Nigeria funded by DFID.
PHE	Public Health England: an executive agency of the Department of Health
POM	Prescription Only Medication
Primary care	Services provided by GP practices, dental practices, community pharmacies and high street optometrists.
Responsible prescribing	The use of antimicrobials in the most appropriate way for the treatment or prevention of infectious disease.
Review on Antimicrobial Resistance	In July 2014, the UK Government commissioned the Review on Antimicrobial Resistance chaired by Jim (now Lord) O'Neill.
SDGs	Sustainable Development Goals
Secondary care	Covers acute healthcare, either elective care (planned specialist medical care or surgery, usually following referral) or emergency care.
Susceptibility testing	Testing to detect possible drug resistance in common pathogens and to assure susceptibility to drugs of choice for particular infections.
TB	Tuberculosis (TB) - a bacterial infection that mainly affects the lungs.
UNGA	United Nations General Assembly
VMD	Veterinary Medicines Directorate - an Executive Agency of Defra.
WHO	World Health Organisation