ANTIMICROBIAL RESISTANCE

Report by Steve Wearne, Director of Policy

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1 SUMMARY

1.1 The emerging resistance of microbes to antimicrobial agents, including those critically important for human therapy, is a significant global threat. There are gaps in the evidence and our knowledge and it is not possible to determine with certainty the contribution that use of antimicrobials in agriculture is making to this issue. However, there is an increasingly robust consensus that unnecessary use of antimicrobials in animals and agriculture is a significant concern, and that minimising the unnecessary and inappropriate use of antimicrobials is an essential component of global strategies to safeguard antimicrobials that are critical for treatment of serious human infections.

1.2 The Board is asked to:

Agree that contributing to efforts to reduce the threat of emerging antimicrobial resistance is aligned with the statutory function and strategic objective of the Food Standards Agency to "protect public health from risks which may arise in connection with the consumption of food, including risks caused by the way in which it is produced"[1];

Agree that, in defining and developing the FSA contribution to UK Strategy objectives on improving knowledge and supporting stewardship, we will act on behalf of consumers' interests relating to food safety and the sustainability of food production and consumption, working with others to encourage the improvements in animal husbandry and biosecurity that will underpin a reduced and more prudent use of antimicrobials in food production animals;

Agree that, in executing the FSA contribution to the UK Strategy we will be clear about our role and responsibilities:

- we will partner with others, acting where we can leverage activity or add value in terms of delivering benefits for consumers, particularly where our role is distinct from those of other partners;
- we will seek out and bring to bear consumers' voices, their interests as consumers and citizens now and in the future, and the opportunities for them to act;
- we will exploit our capability in bridging agricultural production and public health interests: making the case for action; convening and participating in

[1] Food Standards Act (1999), section 1(2).

influential discussions within government, more widely, and internationally; being clear on what is expected of producers, retailers and other players in the food system;

- we will be guided by our strategic objective of providing greater transparency on business standards, including for example the incorporation of criteria for reducing antimicrobial usage within assurance schemes, to incentivise rapid and more comprehensive improvement, support innovation and reward responsible businesses – as well as better informing and empowering consumers.

Note the case study of the reduction in antimicrobial usage by UK poultry processors as an example of the potential for changes in animal husbandry practices to deliver meaningful reductions in antibiotic usage.

2 INTRODUCTION

2.1 The severe nature and potentially huge magnitude of the threat posed by the emerging resistance of microbes to antimicrobial agents is widely accepted. Dr Margaret Chan, Director-General of the World Health Organization said when speaking at a high-level dialogue with UN Member States in April this year[2] that, "the rise of antimicrobial resistance is a global crisis, recognised as one of the greatest threats to health today. The threat is easy to describe. Antimicrobial resistance is on the rise in every region of the world. We are losing our first-line antibiotics. This makes a broad range of common infections much more difficult to treat… With few replacement products in the R&D pipeline, the world is heading towards a post-antibiotic era in which common infections will once again kill… This may even bring the end of modern medicine as we know it".

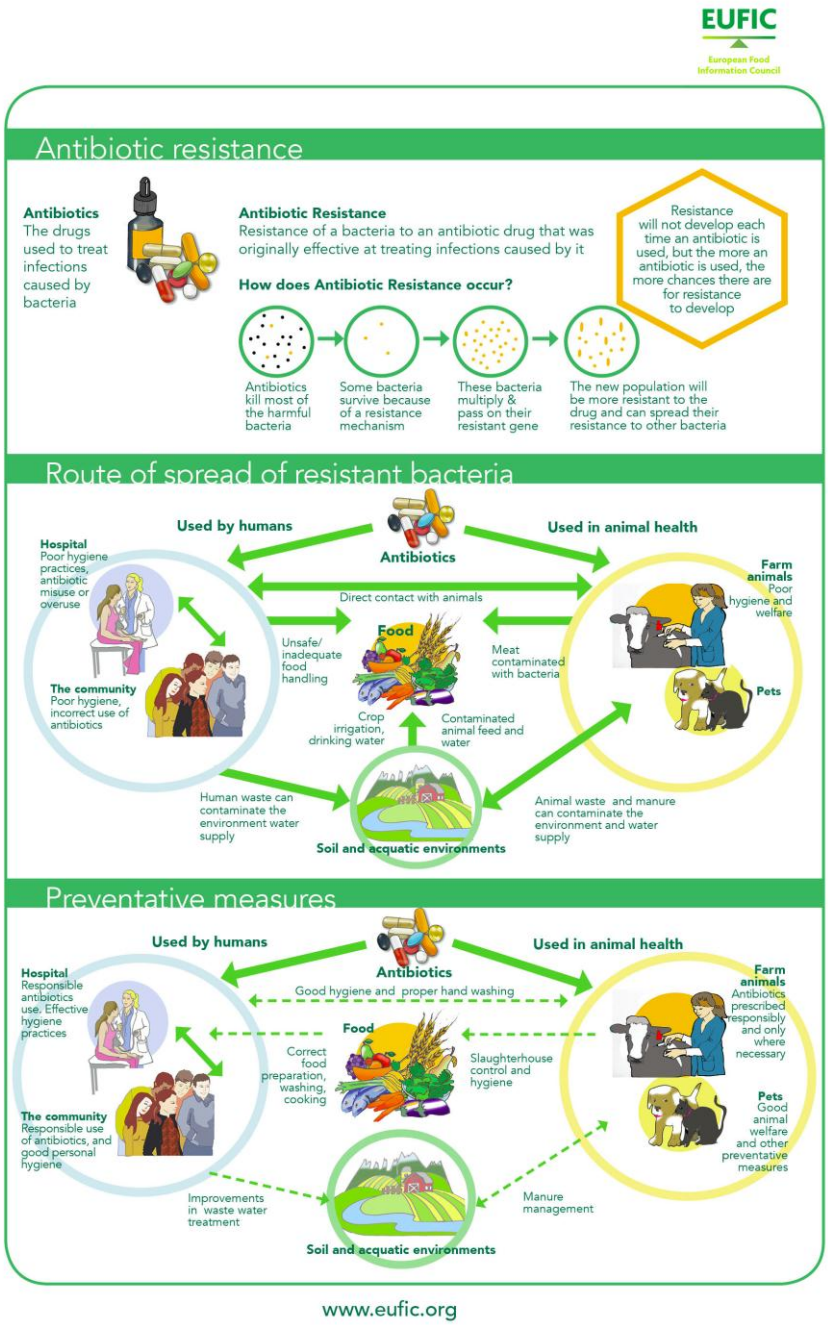
2.2 It is relatively straightforward to identify the pathways by which the use of antimicrobials in animals and agriculture may lead to the emergence of antimicrobial resistant disease in humans (see box 1). Resistant bacteria from animals and humans can transmit in both directions, through human contact with farm, wildlife or companion animals or their environments, through ingestion of contaminated food (both imported and local produced animal and vegetable or fruit items) and through contact with effluent waste from humans, animals and industry. Whilst there is a growing evidence base supporting food as one of a number of transmission routes for antimicrobial resistance, the magnitude of the contribution made by the food chain relative to other source remains to be clarified. Given the size of livestock populations in the UK and globally, the emergence of antimicrobial resistance in agriculture may lead to significant environmental reservoirs of resistant organisms.

2.3 Countering the threat of antibiotic resistance is a priority for the UK Government and the devolved administrations, which are committed to an

[2] See http://www.who.int/dg/speeches/2016/antimicrobial-resistance-un/en/

integrated approach at national and international levels, through actions set out in the UK Five Year Antimicrobial Resistance Strategy[3].

Box 1: Diagrammatic representation of routes for the spread of antibiotic resistance, and potential preventative measures[4]



[3] See https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018

[4] Available at http://www.eufic.org/article/en/rid/ATB_infographic/

2.4 The FSA has been an active partner with other UK Government departments, through the AMR Strategy High Level Steering Group convened by Dame Sally Davies, Chief Medical Officer at the Department of Health, and the AMR Cross-Whitehall International Steering Group convened by FCO. We have built networks and alliances at a senior level, summarised in the Chief Executive's report to the May 2016 Board meeting. We have contributed to the generation of new knowledge on antimicrobial resistance (see section 4.4, below).

2.5 On 19 May 2016, Lord O'Neill published his independent Review on Antimicrobial Resistance,[5] which had been commissioned by the UK Prime Minister in 2014 and conducted in collaboration with the Wellcome Trust. The review report analyses this global problem and proposes concrete actions to tackle it internationally. It makes clear the scale of the challenge (see box 2) and identifies the reduction of "the extensive and unnecessary use of antibiotics in agriculture" as one of four key interventions needed to tackle antimicrobial resistance globally, based on the clear consensus that unnecessary use of antimicrobials in animals and agriculture is a significant concern for human health (see box 3). For food production animals there is the opportunity to improve biosecurity and other husbandry practices to reduce the pressure of infection and as a result decrease the use and consumption of antimicrobials. Minimising the unnecessary and inappropriate use of antimicrobials will reduce the selective pressure that favours the emergence and spread of resistant bacteria. Actions proposed by the Review include:

- ten-year targets, introduced by 2018, to reduce unnecessary antibiotic use in agriculture;
- restrictions and/or bans on agricultural use of certain types of antibiotics that are highly critical in human therapeutic use; and
- improving transparency from food producers on the antibiotics used to raise the meat we eat.

2.6 On 27 May 2016, following the publication of the O'Neill review report earlier that month, the Prime Minister announced,[6] among other commitments, the setting of an overall target for antibiotic use in livestock and fish farmed for food by 2018, cutting use to levels recommended by Lord O'Neill, combined with the strict oversight of the use in animals of antibiotics which are critical for human health – including supporting restrictions or even bans where necessary.

2.7 Improving transparency, as recommended by the Review, is a strategic priority for the FSA and an area where we are well-placed to contribute to the UK Government response to the review. We recognise that greater

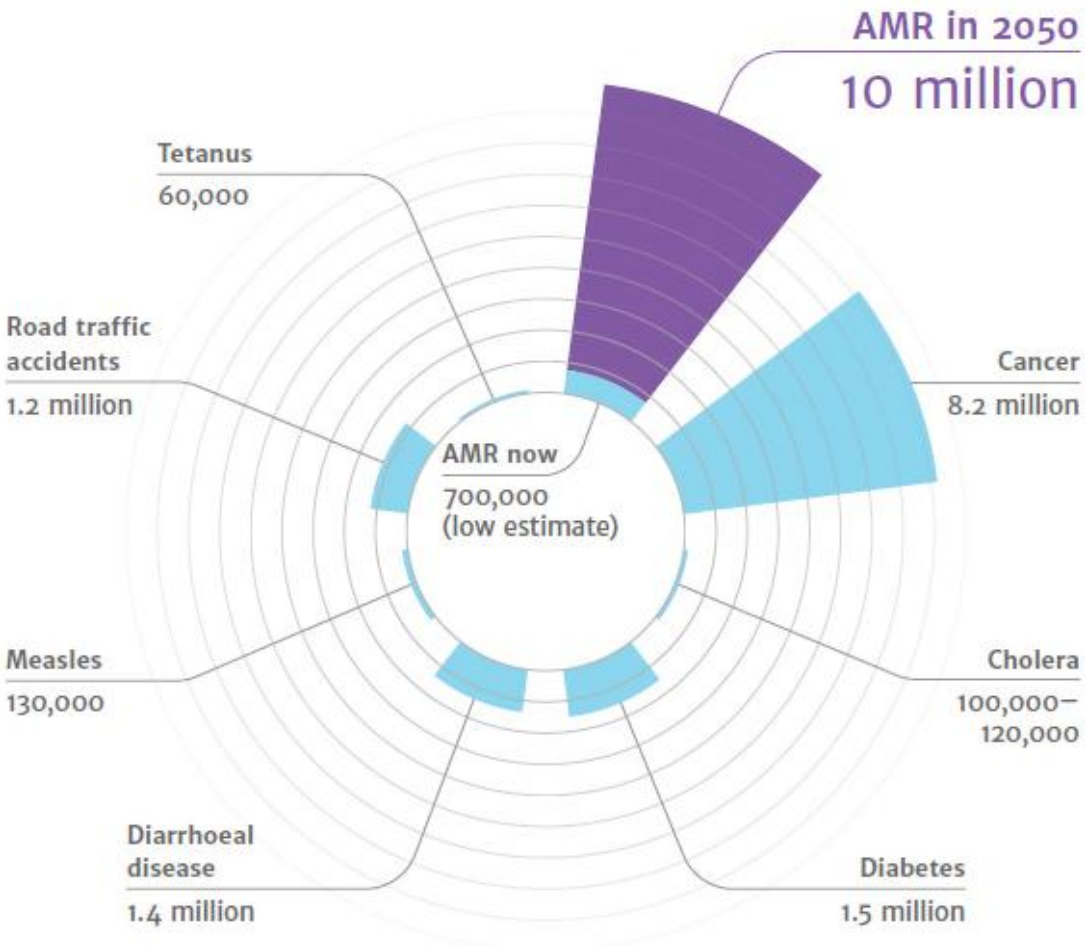
[5] The Review on Antimicrobial Resistance (2016) Tackling drug-resistant infections globally: Final report and recommendations. Available at: http://amr-review.org/
[6] See https://healthmedia.blog.gov.uk/2016/05/27/amr/

transparency will incentivise rapid and more comprehensive improvement, support innovation and reward responsible businesses – as well as better informing and empowering consumers. We will consider the relative merits of different approaches that may be used, including for example the incorporation of criteria for reducing antimicrobial usage within assurance schemes where this can be backed up by robust certification.

Box 2: The scale of the challenge

"We estimate that by 2050, 10 million lives a year and a cumulative US$100 trillion of economic output are at risk due to the rise of drug resistant infections if we do not find proactive solutions now to slow down the rise of drug resistance. Even today, 700,000 people die of resistant infections each year."

Worldwide deaths attributed to various causes:



Box 3: Most published papers provide evidence to support limiting use of antibiotics in agriculture[7]

"It is sometimes suggested that the current evidence is not strong enough to take policy steps now to reduce antibiotic use in agriculture. While we definitely would benefit from more data, generated by better surveillance systems, our research has indicated that the evidence is already compelling.

As part of our analysis, we have undertaken a literature review… The outcomes of this literature review support the proposal that antibiotic use in animals is a factor in promoting resistance in humans...

Of the 280 papers we looked at, 88 (31 percent) were deemed not to be applicable. Of the remaining 192 papers, 114 (59 percent) openly stated or contained evidence to suggest that antibiotic use in agriculture increases the number of resistant infections in humans. Only 15 (eight percent) argued that there was no link between antibiotic use and resistance… Of the 139 academic studies the Review found, only seven (five percent) argued that there was no link between antibiotic consumption in animals and resistance in humans, while 100 (72 percent) found evidence of a link...

In light of this information, we believe that there is sufficient evidence showing that the world needs to start curtailing the quantities of antimicrobials used in agriculture now... given all that we know already, it does not make sense to delay action further: the burden of proof should be for those who oppose curtailing the use of antimicrobials in food production to explain why, not the other way around."

3 STRATEGIC AIMS

3.1 The statutory function of the Food Standards Agency is to protect public health in relation to food and consumers' other interests in relation to food. Our strategy to 2020 takes a wide interpretation on consumers' interests, informed by deliberative consumer research which includes, for example, their interests in being able to choose the food they eat now and in the future, in addition to food being safe and what it says it is.

3.2 There is a food safety risk associated with antimicrobial resistance in pathogens or commensal organisms when found in food. We have conducted risk assessments for Livestock Associated Meticillin-Resistant Staphylococcus aureus (LA-MRSA) in the food chain and Enterobacteriaceae from UK pigs carrying the mcr-1 colistin resistance gene, in each case consulting the Antimicrobial Resistance Working Group of the ACMSF[8]. In each case, we

[7] The Review on Antimicrobial Resistance (2015) Antimicrobials in agriculture and the environment: Reducing unnecessary use and waste. Available at: http://amr-review.org/
[8] For records of the meeting of 29 September 2015 and 4 December 2015 of the Antimicrobial Resistance Working Group of ACMSF, see http://acmsf.food.gov.uk/acmsfsubgroups/amrwg/antimicrobial-resistance-working-group-meeting-29-

have concluded that any risk of human disease resulting from antimicrobial resistant pathogens through meat from animals with these bacteria is very low, when usual good hygiene and thorough cooking practices are observed – although this may be less of a safeguard as people's habits change and the practices of more lightly cooking meats such as pork become more common.

3.3 Therefore, although the immediate food safety risk is very low, the risks to the sustainability of food production systems and future public health more widely are very high, as described in the introduction above.

4 EVIDENCE

The current state of knowledge

4.1 Antimicrobial resistance has been recognised as an emerging risk for some years, and as such has been the subject of a number of authoritative reviews. In 1969 The Report of the Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine (Swann report)[9] found that the administration of antibiotics to farm livestock posed certain hazards to human and animal health since it had led to the emergence of strains of bacteria which are resistant to antibiotics. In 1999 the ACMSF published a comprehensive assessment of the role of antimicrobial resistance in relation to food safety[10] which concluded that there was evidence of transmission of antimicrobial resistance via the food chain particularly for some strains of *Salmonella* and *Campylobacter* infecting humans. Most infections with these organism are self-limiting and do not require antimicrobial treatment unless the infection is more serious.

4.2 Subsequent data from EFSA demonstrates that rates of resistance to fluoroquinolones, a critical class of antimicrobials for human therapy, in *Campylobacter* isolated from poultry, poultry meat and humans has continued to rise, with these rates varying across Europe. Resistance to multiple antimicrobials in *Salmonella* in pigs is also a potential area of concern.[11]

4.3 Foodborne pathogens are not the only source of antimicrobial resistance in the food chain since resistance can arise in, or be acquired by, non-pathogenic (commensal) bacteria including for example, certain strains of *E.coli* and *Enterococcus* spp. Commensal strains of *E.coli* and other bacteria may not necessarily cause disease in humans or animals but they can act as a vehicle for a variety of drug resistance genes some of which can be passed to other bacteria. These recipients may then cause serious disease often in

september-2015 and http://acmsf.food.gov.uk/acmsfsubgroups/amrwg/antimicrobial-resistance-working-group-meeting-4-december-2015

[9] Swann, M.M., Baxter, K.L., Field, H.I. et al (1969) Report of the Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine. Publ. HMSO, London.

[10] ACMSF (1999) Report on Microbial Antibiotic Resistance in Relation to Food Safety. Publ. The Stationary Office, London.

[11] European Food Safety Authority and European Centre for Disease Control (2015) EU Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013. EFSA Journal 13: 4036.

sites other than the gastrointestinal tract. One example of this phenomenon is the *mcr-1* gene for colistin resistance which was first reported from food animals, meat and humans in China in November 2015[12] and has now been found in many countries worldwide. Colistin is one of the very few antimicrobial drugs of last resort and there is a concern that colistin use in animal production could drive the horizontal spread of the *mcr-1* gene to reach pathogens for which there may be no other treatment option apart from colistin.

4.4 Current research funded or part-funded by the FSA includes:

- A systematic review of the occurrence of antimicrobial resistance in pathogens and commensals in retail food, due to be published in September 2016.

- Rolling surveillance of retail meats in the UK as part of a wider programme of EU surveillance for antimicrobial resistance.[9]

- A three-year multidisciplinary study on defining reservoirs of ESBL-producing *E.coli* and the threat posed to personal, animal and public health in the UK, due to be published later this year.

Evidence gaps

4.5 Our understanding of the ecology and transfer of antimicrobial resistant bacteria in the food chain is improving but remains incomplete. Differences in surveillance systems, methodology and target organisms and drugs often make it difficult to align information and make comparisons particularly between countries or at different times. Understanding better the role that food and food production animals play in the spread of antimicrobial resistant organisms and genes will require the development and application of scientific predictive methods and models that quantify the transfer of antimicrobial resistant commensal and pathogenic organisms and genes along the food chain from primary production to consumer.

4.6 Emerging findings from the systematic review we have commissioned suggest a relative paucity of high quality information on the prevalence of antimicrobial resistance in bacteria on UK retail food. We will prioritise improving the information available on this topic as we develop our new strategic approach to surveillance.

[12] Liu, Yi-Yun et al. (2015) Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. The Lancet Infectious Diseases 16: 161-168.

5 DISCUSSION

5.1 The UK Five Year Antimicrobial Resistance Strategy has the goal of slowing the development and spread of antimicrobial resistance, focusing action across all sectors on:

- improving the knowledge and understanding of antimicrobial resistance;
- conservation and stewardship of the effectiveness of existing treatments; and
- stimulating the development of new antibiotics, diagnostics and novel therapies.

5.2 There needs to be clarity about roles and responsibilities around the spectrum of policy and action on antimicrobial resistance. On occasion the FSA may have a leadership role and on other occasions a supporting role. We are concerned to avoid confusion and duplication on the complex efforts to tackle antimicrobial resistance here and globally, and will continue to work constructively to play the full suite of roles that fall to the FSA as a partner in the community facing this challenge.

5.3 Accordingly, in defining and developing our contribution to objectives on improving knowledge and supporting stewardship, we will act on behalf of consumers' interests relating to food safety and the sustainability of food production and consumption, working with others to encourage the improvements in animal husbandry and biosecurity that will underpin a reduction and more prudent use of antimicrobials in food production animals. In executing the FSA contribution to the UK Strategy we will be clear about our role and responsibilities:

- we will partner with others, acting where we can leverage activity or add value in terms of delivering benefits for consumers, particularly where our role is distinct from those of other partners;
- we will seek out and bring to bear consumers' voices, their interests as consumers and citizens now and in the future, and the opportunities for them to act;
- we will exploit our capability in bridging agricultural production and public health interests: making the case for action; convening and participating in influential discussions within government, more widely, and internationally; being clear on what is expected of producers, retailers and other players in the food system;
- we will be guided by our strategic objective of providing greater transparency on business standards, including for example the incorporation of criteria for reducing antimicrobial usage within assurance schemes, to incentivise rapid and more comprehensive improvement and

reward responsible businesses – as well as better informing and empowering consumers.

A case study – reducing the use of antimicrobials by the UK poultry industry

5.4 The quantity of antibiotics used in livestock is vast. Recent estimates indicate that in the US, of the total volume by weight of antibiotics defined as medically important for human therapy, over 70% are sold for use in animals. In many other countries this information is not held or published.

5.5 In the UK, data on sales of antibiotics for use in animals is collected by the Veterinary Medicines Directorate (VMD). The most recent data[13] indicate that sales of antibiotics for use in food-producing animals in the UK increased by 4% between 2013 and 2014 and remain above the baseline of average annual sales between 2008-2012 (see box 4), although when corrected for changes in livestock population, usage has remained stable. There is in general no consistently good information on use in different animal species, and improving data for key livestock sectors (pigs, poultry and cattle) remains a priority for VMD. The exception to this is antibiotic usage in poultry reared for meat, where data on usage collected by the British Poultry Council indicates a decrease from 93 tonnes to 62 tonnes between 2013 and 2014. This makes it possible to estimate combined usage in egg-producing flocks, game birds and pigs (the majority of which will arise from use in pigs), which increased from 213 tonnes to 246 tonnes between 2013 and 2014, and usage in other food producing animals (including cattle), which increased from 49 tonnes to 61 tonnes over the same period.

Box 4: Antibiotic ingredient sale for use in food-producing animals in the UK

	2008-2012 (range)	**2013**	**2014**
Tonnes of antibiotic ingredient sold for use in			
Food producing animals	347 (290-390)	355	369
Meat poultry (usage data from BPC)	NA	93	62
Balance of sales authorised for use in pigs and poultry	NA	213	246
Balance of sales for all food producing animals	NA	49	61

5.6 The total antibiotic usage data indicate the leadership that the UK poultry sector has demonstrated in reducing antibiotic usage. The British Poultry Council Antibiotic Stewardship Scheme, established in 2011, published a report[14] in April 2016 which sets out its achievements to date. These include:

[13] Veterinary Medicines Directorate (2016) Animal Health: Actions and Progress in Reducing the Threat of Antibiotic Resistance 2013-2018 (in press at time of writing)
[14] See http://www.britishpoultry.org.uk/bpc-antibiotic-stewardship-scheme-publishes-data-demonstrating-successful-responsible-use-strategy/

- being the first UK livestock industry to pioneer a data collection mechanism to record antibiotic usage covering 90% of the production across the sector, and sharing this data with UK Government;
- in 2012, introducing a voluntary ban on the use of third and fourth generation cephalosporins, and a commitment to reduce the use of fluoroquinolone antibiotics;
- in 2016, making a further commitment to not use colistin; and
- between 2012 and 2015, when there was a 5% increase in UK production of poultry meat, overseeing a reduction in the total usage of antibiotics in the UK poultry sector by 44%.

5.7 Reg Smith of the major poultry processor Faccenda, who chairs the stewardship scheme, has been invited to give a short presentation to the Board on the work of the scheme and will be available to answer questions from Board members.

5.8 We recognise that countering the threat of antimicrobial resistance requires action at pace by all. We are joining with others across government to implement the UK Strategy and to make the case for action globally. In terms of domestic UK food production, action is required in every sector.

5.9 As part of the FSA contribution to the UK Strategy, we will look to exploit our capability in bridging agricultural production and public health interests to make the case for parallel action in pig and cattle sectors, convening and participating in influential discussions within government and more widely, and being clear on what is expected of producers, retailers and other players in the food system.

5.10 We recognise that action to reduce use of antimicrobials in agriculture will require changes to husbandry and biosecurity practices that reduce the prevalence and incidence of diseases that require treatment with antimicrobials. These improved controls would be likely to increase costs in the short term, which may lead to increases in price for some foods. In terms of benefits, in addition to reductions in the emergence and amplification of antimicrobial reduction, we would also expect gains in animal health and welfare through reduction of disease, and a more efficient use of feed resulting in more sustainable production.

6 DEVOLUTION IMPLICATIONS

6.1 The UK Five Year Antimicrobial Resistance Strategy, which provides the framework for FSA work in this area, is jointly supported by UK Government departments and the devolved administrations.

6.2 We continue to work closely with Food Standards Scotland on action to bridge between agricultural and public health interests. The objectives of FSA and FSS are complementary, and one of the proposals in the FSS draft foodborne illness strategy is to incorporate a more integrated ‘One Health’ approach to reduce pathogen risks in Scotland in the context of veterinary, environment,

water and foodborne transmission, which will help us to better understand the emergence and impact of antimicrobial resistance.

7 CONSUMER ENGAGEMENT

7.1 We commissioned an initial online omnibus survey of 1263 adults in May 2016 to assess consumers' awareness, concern and knowledge of antimicrobial resistance.

7.2 Of the people surveyed:

- 74% had heard of "superbugs" (highest among those aged 55+) ;
- 61% had heard of antibiotic resistance;
- 16% had heard of antimicrobial resistance (highest among those aged 16-24);
- 11% had heard of AMR;
- 16% had heard of none of these terms.

Of those aware of any of those terms, 72% were concerned about antimicrobial/antibiotic (AM/AB) resistance from people taking too many antibiotics and 62% were concerned about AM/AB resistance within the food chain.

7.3 We asked participants whether headline statements relating to antimicrobial resistance were true or false, and in each case the majority of respondents identified the correct answer (see box 5).

Box 5: Responses from an online omnibus survey of UK adults, when asked whether statements relative to antimicrobial resistance were true or false

Statement	True	False	Don't know
Illness caused by AM/AB resistant bacteria may not be able to be treated with medicine	57%	11%	32%
Infection with AM/AB resistant bacteria could make me ill	71%	6%	23%
Spread of AM/AB resistant bacteria will make us better at resisting illness	12%	51%	37%
Routine medical processes will become more dangerous in AM/AB resistant bacteria spread	69%	6%	25%

7.4 We will develop plans for further consumer engagement, to allow us to seek out and bring to bear consumers' voices and concern, in line with the principles that will underpin the execution of our contribution to the UK Strategy, and to inform our communication to consumers.

7.5 We recognise the potential for activated and empowered consumers to take action not only through their choices about the food they buy and eat, but also as citizens, for example in supporting decisions already being made by the institutional investors to whom they have entrusted with their savings and pensions.[15]

8 CONCLUSION AND RECOMMENDATIONS

8.1 The Board is asked to:

Agree that contributing to efforts to reduce the threat of emerging antimicrobial resistance is aligned with the statutory function and strategic objective of the Food Standards Agency to "protect public health from risks which may arise in connection with the consumption of food, including risks caused by the way in which it is produced";

Agree that, in defining and developing the FSA contribution to UK Strategy objectives on improving knowledge and supporting stewardship, we will act on behalf of consumers' interests relating to food safety and the sustainability of food production and consumption, working with others to encourage the improvements in animal husbandry and biosecurity that will underpin a reduced and more prudent use of antimicrobials in food production animals;

Agree that, in executing the FSA contribution to the UK Strategy we will be clear about our role and responsibilities:

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- we will be guided by our strategic objective of providing greater transparency on business standards, including for example the incorporation of criteria for reducing antimicrobial usage within assurance schemes, to incentivise rapid and more comprehensive improvement, support innovation and reward responsible businesses – as well as better informing and empowering consumers.

[15] 'Systemic' antibiotics crisis troubles big investors, Financial Times, 10 April 2016. Available at: https://next.ft.com/content/13c5a55a-fd7e-11e5-b5f5-070dca6d0a0d

Note the case study of the reduction in antimicrobial usage by UK poultry processors as an example of the potential for changes in animal husbandry practices to deliver meaningful reductions in antibiotic usage.