Anitibiotic Resistance 101

food&water europe

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Antibiotics are critical tools in human medicine, and we all have good reason to be worried about losing them. Medical authorities warn that these life-saving drugs are losing their effectiveness, and there are few new drugs in the pipeline to replace those that no longer work because the bacteria that make people and animals ill are no longer susceptible to the drugs.[1] According to Public Health England (PHE), “It has been 30 years since a new class of antibiotics was last introduced. Only three of the 41 antibiotics in development have the potential to act against the majority of the most resistant bacteria.”[2] PHE estimates that failure to address antibiotic resistance (AR) could result in 10 million deaths per year worldwide by 2050.[3]

The Food and Agriculture Organization of the United Nations (FAO) calls antibiotic resistance “one of the most serious risks to human health at the global level”.[4] The news in 2015 that bacteria resistant to colistin, the antibiotic of last resort used when other drugs fail, have been found in a number of countries worldwide heightened concern that the predicted post-antibiotic era may be approaching more rapidly than imagined (see box on page 5).

Food & Water Europe is fighting to stop the farming practices that threaten the effectiveness of our antibiotics. This briefing paper explains the problem from a European perspective and outlines what needs to be done. For further information about the situation in the United States, see the Food & Water Watch report *Antibiotic Resistance 101.*

Antibiotic resistance

All species evolve and adapt in response to their environment over time. Bacteria reproduce rapidly, encouraging faster adaptation. Antibiotics kill bacteria, but if a few bacteria withstand the treatment and survive, when they reproduce, they pass on the traits that allowed them to resist the antibiotics. The new generations of bacteria will be resistant and will not be killed by the antibiotic. Any use of antibiotics to some degree leads to resistance in this way,[5] and antibiotic resistance has become a global problem.[6]

Infections involving AR bacteria make people increasingly ill because it takes multiple rounds of increasingly stronger antibiotics to treat them, allowing the infection to progress

Definitions

With many organisations and companies, including for-profit vested interests, discussing antibiotic resistance in many languages and settings, it is very important to ensure clarity of terms. Food & Water Europe uses the following definitions:

- Antimicrobial: any compound with a direct action on microorganisms that is used for treatment or prevention of infections. Antibiotics are a type of antimicrobial.
- Curative (therapeutic) treatment: treatment of an ill animal or group of animals, when the diagnosis of disease or infection has been made.
- Preventive treatment (prophylaxis or nontherapeutic treatment): treatment of an animal or a group of animals before clinical signs of disease emerge. This includes routine use of medicines where no disease is present in order to prevent its emergence and for all other purposes, like increasing weight gain, that are not disease management.

further than it might have done if the original treatment still worked. Diminishing numbers of drug options can also make it harder for doctors to treat patients with allergies to some antibiotics and make it more likely that patients will require stronger drugs administered intravenously.[7]

Given this inevitable trend, it is important to find ways to maintain the effectiveness of antibiotics for as long as possible. Unfortunately, the livestock industry uses antibiotics in ways that contribute to the emergence and spread of AR bacteria.

How industrial agriculture abuses antibiotics

Many livestock producers and fish farmers use antibiotics appropriately to treat sickness in accordance with their moral and legal obligations to the animals in their care.

However, since the 1950s, antibiotics have been used in agriculture for routine, low-dose nontherapeutic (e.g., preventative, or prophylactic) disease prevention, and in some places, including the United States, for growth promotion (a practice now banned in the EU), particularly in densely packed and unsanitary factory farms.[8] Far more antibiotics are given to livestock than to people,[9] and the livestock taking them usually are not sick. This practice accelerates the development of the AR bacteria now threatening human health.[10]

Whereas appropriate treatment of sick animals is less likely to contribute to resistance, routine nontherapeutic use over long periods of time creates conditions that promote the development of AR bacteria by killing the bacteria susceptible to the drug but leaving the AR bacteria to survive and reproduce.

The use of even one antibiotic in this manner can select for resistance to multiple classes of antibiotics, because the genetic trait that allows bacteria to survive exposure to one antibiotic is often linked to traits that allow it to survive others.[11] It is therefore worrying that drugs used nontherapeutically for animals come from every major class of antibiotics used in human medicine.[12] Many drugs used for nontherapeutic purposes are also used for disease treatment in both veterinary and human medicine, and many AR genes are already widespread.[13]

Estimates differ on precisely how many antibiotics are used in agriculture generally or for nontherapeutic purposes specifically. There is no centralised system for collecting such data. The pharmaceutical industry is not eager to share such business information.[14]

Bearing this in mind, estimates of global antibiotic use in livestock production range from 63,000 tonnes to over 240,000 tonnes annually.[15] The independent Review on Antimicrobial Resistance commissioned by the UK Government (the O'Neill Report) accepts that most countries use more than 50 percent of their antibiotics in livestock production.[16] In the United States, Food and Drug Administration (FDA) data indicate that, in 2011, 80 percent of antibiotics sold in the country were used for agriculture,[17] with 70 percent of those used in livestock sold for use in feed and 24 percent for use in water.[18] In the UK, the total antibiotics dispensed in 2013 to humans was 531 tonnes and total sales for animal use was 419 tonnes (approximately 40 percent of total use).[19]

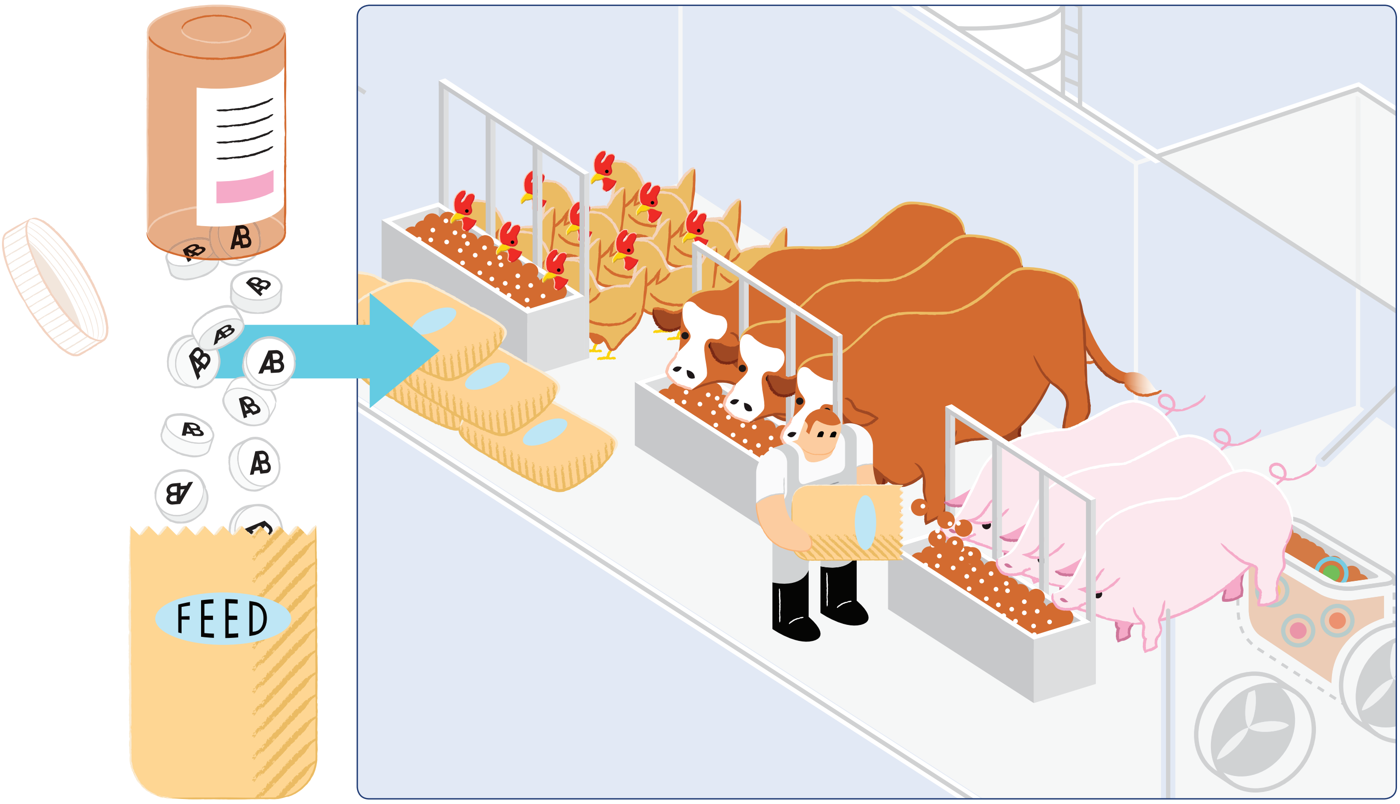
In aquaculture, antibiotic doses can be proportionately higher than in livestock, leaving residues in food and up to 70-80 percent of the antibiotics used in aquaculture excreted into the environment.[20] Antibiotics are less effective in sea water, potentially forcing required doses up by as much as 60-fold.[21] Given that the FAO says, "Antibiotics have not always been used in a responsible manner in aquaculture and, in a number of reported situations, control of the use of antibiotics has not provided an adequate assurance of the prevention of risk to humans,"[22] we may know even less about the full extent of the problem at sea than we do on farms.

While direct conclusions are difficult to draw based on the amounts of antibiotics used alone, it is clear that a significant proportion of global antibiotic use is in food-producing animals, and a good deal of that goes to animals that are not sick, at a time when resistance is a growing problem for both human and veterinary medicine.

How antibiotic-resistant bacteria spread in the environment

Not only do AR bacteria become more numerous in response to selective pressure by reproducing more copies of themselves, but they also can share the resistance genes with neighbouring bacteria.[23] This process, called horizontal gene transfer, allows both faster spread of AR genes and easier acquisition of resistance to multiple drugs by multiple types of bacteria.[24]

These resistance genes, no longer tied to a specific species of bacteria, persist in the wider microbial environment,



creating reservoirs of resistance in which resistance genes become widespread and can be acquired by other bacteria through repeated horizontal gene transfer.[25] Once AR genes have developed, they spread easily and are exceedingly hard to control, and have even been called “highly promiscuous” because of this.[26]

Gene transfer can occur among the bacteria in animal digestive tracts and then spread via waste into the environment,[27] so reservoirs of AR bacteria persist in livestock and in the environment around farms. In large livestock operations, manure is collected in lagoons,[28] where fecal bacteria can survive for months outside the animal.[29] Most of the antibiotics fed to livestock are also excreted in waste, adding an additional low-level exposure to bacteria in the lagoon and in the environment, perpetuating the further development of AR bacteria.[30] Several studies have found DNA matches between AR bacteria in the soil and water and in manure lagoons.[31]

Neither lagoon storage nor anaerobic digestion, a process used to convert livestock waste into energy, significantly decreases the presence of AR genes.[32] Poultry litter has also been found to harbor multiple-drug-resistant *E. coli* and antibiotic residues.[33] Any waste treatment to reduce bacteria levels that only partially eliminates bacterial contamination can be rendered ineffective when the bacteria simply grow back.

Since most livestock waste is spread on the land as fertiliser, AR bacteria are introduced into the local environment,[34] creating the possibility for horizontal transfer of resistance genes to bacteria in fields, streams, ponds and groundwater. These bacteria can then carry on reproducing with these new traits and contributing to the reservoir of antibiotic resistance.[35] Furthermore, vehicles carrying livestock leave AR and other bacteria in the air behind them,[36] and flies attracted to livestock waste pick up and may disperse AR bacteria.[37]

While there is disagreement about the degree to which antibiotic use in agriculture contributes to the development of resistant bacteria, research establishing the links is clear. In the United States, Spain and the Netherlands, researchers found 8- to 16-fold increases in AR *Campylobacter* within just three years of the introduction of the antibiotic class fluoroquinolone in poultry.[38] A 2011 trial took piglets from the same litter and raised them in two groups under the same conditions, except that one group was given low doses of antibiotics in the feed.[39] After only two weeks, the treated piglets developed significantly higher levels of AR *E. coli*. The AR *E. coli* in the treated piglets carried a higher variety of AR genes, including some that conferred resistance to drugs not used in the study.[40] Higher concentrations of AR bacteria were found downwind of hog facilities a few weeks after hogs received a dose of nontherapeutic antibiotics.[41]

From livestock to farmers, from meat to consumers

The European Medicines Agency (EMA) says, “The majority of *Salmonella spp.* and *Campylobacter spp.* causing human infections in EU Member States are zoonotic in origin [transferring from animals to people] and most likely originate in food production animals.”[42] Studies have found that resistant bacteria in livestock spread to farmers, farmworkers and rural residents.[43]

In poultry production, as early as 1976, researchers found that AR bacteria spread rapidly in the intestines of chickens raised using nontherapeutic antibiotics. Farmers on the same poultry operations developed higher levels of AR bacteria in their intestinal tracts compared to their neighbours.[44] Multiple studies have identified the similar strains of AR bacteria in farmers and their livestock.[45] A study of poultry workers found a strain of *E. coli* resistant to gentamicin to be 32 times higher in the workers compared to other members of the community, with half of the poultry workers carrying the AR strain.[46]

In pig production, strains of methicillin-resistant *Staphylococcus aureus* (MRSA) have been found in both pigs and the people who raise them.[47] One strain of MRSA has been found in both pigs and the people who raise them, but not in neighbours who do not raise pigs.[48] Two studies have found farmworkers and pigs carrying the same strains of MRSA on conventional livestock farms, but not on farms that do not use antibiotics in raising livestock.[49] Research shows an increased likelihood of MRSA skin infections in people living near fields treated with swine manure.[50] A study by 20 institutes studying 89 genomes from humans and animals in over 19 countries[51] showed that the strain of MRSA associated with livestock originated in humans, transferred to pigs where it acquired resistance to tetracycline and methicillin, and then jumped back to humans.[52]

When European doctors found increasing rates of vancomycin-resistant infections in hospital patients during the 1990s, researchers found the same resistance patterns in AR bacteria in meat and manure.[53] The EU responded by restricting vancomycin use in agriculture, and rates of vancomycin-resistance in people fell. The United States never approved vancomycin for nontherapeutic uses in livestock, and, while resistant *Enterococcus* infections do occur in U.S. hospitals, the problem has never been as great as the point reached in the EU.[54]

While there is still argument from the meat and pharmaceutical industries about how much of the AR problem is caused by antibiotic use in food production, the link is increasingly hard to deny. A 2015 review of 280 published, peer-reviewed articles found "compelling" evidence that antibiotic use in animals is a factor promoting resistance in humans, with only 8 percent of the papers reviewed arguing that there is no link.[55]

One way that resistant bacteria infect us is via our food, and there is a decent chance that meat or chicken bought at a supermarket has AR bacteria on it, putting you and your family at risk. The World Health Organization (WHO) report on antibiotic resistance and food safety in Europe confirms, "Food products of animal origin are often contaminated with bacteria, and thus likely to constitute the main route of transmitting resistant bacteria and resistance genes from food animals to people."[56] The EMA agrees, saying, "[A]ntimicrobial resistance is increasing among *campylobacter* infections and is common among isolates from other sources, specifically retail poultry meat."[57]

Moreover, according to the EMA and WHO, modern travel and international trade contribute to the spread of the resistance problem over long distances.[58]

Even occasional transmission to humans can have a significant negative impact because of the way resistance genes spread.[59] People can carry AR bacteria for years without realising it, and those same AR bacteria can pose grave danger as an infection.[60] Antibiotic resistance has become such a serious problem that there are few or no treatment options in some cases,[61] and pharmaceutical companies are not producing new treatments fast enough to keep up with the need.[62]

The results can be serious, and the arrival of bacteria resistant to our antibiotic of last resort, colistin, threatens to make things worse (see box). According to the European Centre for Disease Prevention and Control and the EMA, the situation is already sobering: "[A]t least 25,000 patients in the EU each year die from infections due to multidrug resistant bacteria."[63] The European Commission says that treating multidrug-resistant infections costs European healthcare systems and productivity at least an extra €1.5 billion per year.[64] These numbers reflect costs from total AR illnesses.

Some of these infections may be caused by bacteria that people are exposed to not via food, but from the wider environment. The point is that agricultural misuse of antibiotics is driving the creation of the AR bacteria, which are then spread generally through the wider environment. This means that we all may be exposed to, and pay the price for, dangerous AR bacteria that are the result of agricultural misuse of antibiotics, even if we don't eat meat or live near a farm.

To put this in perspective, in the UK alone, *E. coli* was the most common cause of human bloodstream infections in 2013, with 35,716 reported cases.[65] Of these, 18 percent were resistant to Ciprofloxacin (a drug used to treat, among other things, anthrax[66]), and 10 percent were resistant to both Cefotaxime (uses include meningitis treatment[67]) and Ceftazidime (uses include meningitis and pneumonia treatment[68]).[69]

In animal *E. coli* infections in the UK, 11 percent were resistant to Cefotaxime and 6 percent were resistant to Ceftazidime, which is worth noting because neither drug is authorised for use in animals,[70] so the resistance should not have been acquired through overuse of the drug in animals.

Campylobacter gastroenteritis was the most common human-acquired bacterial zoonosis (infection in animals that can be transmitted to humans) in the UK in 2013.[71] Results for antibiotic resistance tests are available for 45 percent of the 66,575 reported cases; 42 percent of those were resistant to Ciprofloxacin and 2.5 percent resistant to erythromycin (used for patients who can't take penicillin[72]).[73] In 2014, zoonotic infections of both *Campylobacter* and *Salmonella* in humans increased in the UK, reversing previous downward trends, and confirmed cases of one type of *E. coli* showed "a significant increase".[74]

In the United States, the Centers for Disease Control and Prevention estimates that at least 2 million Americans each year experience AR infections, leading to at least 23,000 deaths.[75] Approximately 22 percent of those infections originate from foodborne pathogens.[76]

The last resort under threat

Colistin resistance is a good example of why a conservative approach to antibiotics is prudent — what we know today may not hold tomorrow, and by the time the need for action is identified and implemented, it may be too late.

Colistin was first used in Europe in the 1950s,[77] including to prevent diarrhoea in pigs,[78] but its use in humans was restricted because of its toxicity.[79] According to the EMA, colistin resistance was known but was reported to be "in theory non-transferable".[80] The EMA reports, "Colistin has been used regularly in veterinary medicine for decades, both as curative treatment and for prevention of disease,"[81] and, by 2012, "Colistin accounted for more than 30 percent of the antimicrobial use in swine and 15 percent in veal farming."[82] In 2010, the use of colistin in poultry production was touted in the veterinary press for its ease of administration and "almost zero levels of resistance, even with bugs variously resistant to other antimicrobials".[83]

By July 2013 things had changed, and the EMA said that colistin now plays "a key role for public health", adding, "Due to the critical importance of colistin for use in human medicine, there is a need to focus on the possible consequences of veterinary use of colistin for human public health."[84] PHE reports that colistin use for human patients is high in England compared with other European countries, increasing 20 percent between 2013 and 2014 "in response to a high prevalence and increasing life expectancy of cystic fibrosis patients, as well as growing numbers of multi-resistant bacterial isolates causing serious infections".[85] The rise of antibiotic resistance had helped turned colistin from a drug used only in animals into a medicine of last resort for otherwise untreatable human conditions.

(continued on page 6)

Tackling antibiotic resistance

Halting the development and spread of AR bacteria is vital for the preservation of antibiotic effectiveness in both human and veterinary medicine. Strong food safety practices are particularly important to prevent AR bacteria and disease outbreaks, but a comprehensive farm-to-fork system of control is needed, including a ban on all routine nontherapeutic antibiotic use in food-producing animals, improved monitoring and reporting of emerging resistance and improved environmental protections. It is critical to prevent the emergence and spread of AR bacteria among food-producing animals to minimise the entry of AR bacteria into the food supply, particularly as global trade and air travel provide clear vectors for resistance and disease to spread increasingly easily.

By far the best way to prevent the spread of AR bacteria is to prevent their development in the first place, and it is more effective to take action when AR bacteria first emerge than to wait until the trait becomes widespread and threatens animal or human health.[101] Once AR traits spread via horizontal gene transfer throughout the ecosystem, the AR trait may be virtually impossible to eradicate and may persist for many years.[102] This is why eliminating nontherapeutic uses of antibiotics can make a difference in reducing the prevalence of AR bacteria,[103] but it may not stop the spread of AR bacteria

The last resort under threat *(continued from page 5)*

The timeline of developments in late 2015 shows how easily official responses can be outpaced by real-world developments:

9 October 2015: The UK Advisory Committee on Animal Feedingstuffs agreed with the July 2013 EMA advice that preventative use of colistin in animals should be halted.[86]

18 November 2015: A Chinese study revealed that between 2011 and 2014 transferable colistin-resistant E. coli were present in 15 percent of raw meat samples, 21 percent of animals tested and 1 percent of infected hospital inpatients.[87]

22 November 2015: Twenty senior medical experts published a letter in *The Times* calling for an official end to group nontherapeutic use of antibiotics in animals in feed and water.[88]

26 November 2015: The British Veterinary Association (BVA) called for a "proportionate response" to the Chinese study. BVA Senior Vice President John Blackwell said, "It would be pragmatic to carry out new risk assessments."[89]

3 December 2015: The UK Department of Health was asked formally in Parliament for a statement and replied on 8 December, "While PHE and the Food Standards Agency judge that the public health risk of colistin-resistant bacteria from slaughtered animals and the food chain is very low, the use of colistin for animals will be reviewed following recent reports of transferable colistin resistance in China and Europe."[90]

4 December 2015: The Responsible Use of Medicines in Agriculture group (RUMA) announced voluntary restrictions on colistin to use only as a medicine of last resort while an EU risk assessment is conducted.[91] Despite earlier assurances that such resistance was believed to be "non-transferable", in early December the British Society for Antimicrobial Chemotherapy called the discovery of colistin-resistant bacteria in one patient and food from Denmark "worrying", adding that the fact that samples dated back to 2012 "means that this type of resistance may be widespread".[92]

11 December 2015: The EMA sought a mandate from the European Commission to review and update its 2013 advice on colistin.[93] News emerged that transferable colistin-resistance traits had been found in 15 samples from UK pig farms, imported meat and human patients.[94] Subsequent media reports said the problem is present in France, the Netherlands, Portugal and parts of Asia and Africa in addition to China, Denmark and the UK.[95]

The UK press reports were based on a 7 December 2015 PHE notification that, following the Chinese revelations, UK agencies had ordered the evaluation of 24,000 archived samples.[96] Initial results found transferable colistin-resistant bacteria in samples dating back to 2012, confirming that the problem "is already present in England and Wales in various bacterial species harboured by the human population", and that other resistance genes were also found.[97]

Indeed, as transferable colistin resistance was already present in 2012 in both Denmark and the UK, even the 2013 EMA recommendation that preventative colistin use in livestock be halted was tardy. Medical predictions in 2015 that it would be "three years before colistin resistance would spread from China to the UK" were exposed as woefully complacent.[98] It was already in the UK, and elsewhere in Europe, overlooked by inadequate monitoring and potentially aggravated by continued nontherapeutic antibiotic use in animals.

Remarkably, John Blackwell echoed the BVA's minimalist approach even after the colistin-resistant strains were identified in the UK, noting that prescribing practices in human medicine are the "main drivers" for the development of drug resistance in the human population.[99] While this may or may not be true, the vital importance of antibiotics to both human and veterinary medicine, coupled with the changes over time in the importance of individual medicines as resistance develops and spreads, means that we must take all action possible to delay the day when antibiotics fail across the board. Quibbling about how much agriculture contributes to the rise of resistance is not enough when there are other, better options.

Laura Piddock, Professor of Microbiology at of University of Birmingham and Director of the global group Antibiotic Action, says: "The use in farms should be minimised and alternative treatments found.... When it comes to colistin in particular, it's one of those cases where we are now reusing it in human medicine, and therefore we want to reclaim it from the vets. This new-type resistance has come upon us very quickly. We still don't know the real impact on human medicine."[100]

that already exist.[104] Vigilance will already be required for many years to come; we should not make the problem worse.

Sadly the U.S. livestock industry still minimises its role in antibiotic resistance.[105] In Europe, many adopt an "as much as necessary, as little as possible" approach that does not clearly rule out routine nontherapeutic use (see box).[106] Groups taking such a stance could help us all by taking clear positions against the use of routine nontherapeutic antibiotic use to differentiate their organisations from those that still support such uses.

Animals can be raised successfully without nontherapeutic antibiotic use, and this has the clear benefit of not adding to the reservoir of resistance. Raising livestock without nontherapeutic antibiotics requires changes in herd management, including lowering animal density and changing nutritional programmes.[107] Animals crowded into factory farms may face increased stress and poor hygiene, which facilitates the spread of pathogens and slows animal growth. Minimising livestock stress and maximising hygiene can therefore provide growth-promotion and infection-prevention benefits without the nontherapeutic use of antibiotics.

Two years of changed practices can be sufficient to begin to show improvements in the level of resistance in bacteria in livestock and meat.[108]

Europe has good experience with radically reducing antibiotic use in agriculture, including:

- In 1986, Sweden became the first EU country to ban the use of antibiotics as growth promoters. Sweden's livestock producers faced increases in livestock disease immediately after the ban, but government data showed no decrease in production due to the ban.[109]
- Danish hog farms experienced a brief spike in therapeutic antibiotic use in swine after banning antibiotics for growth promotion,[110] but between 1992 and 2008, Danish pig farmers increased production by nearly 40 percent while antibiotic use per pig dropped by 50 percent.[111] Extensive government tracking of AR bacteria and antibiotic use in animals and humans has been key to Denmark's success.[112]
- In addition to banning nontherapeutic uses of antibiotics, the Netherlands tracks all antibiotic use on farms by veterinarians and enforces fines for overuse.[113] Sales of antibiotics for veterinary purposes have decreased by 58 percent since 2009, surpassing the government goal of a 50 percent reduction, and antibiotic resistance trends in animals have improved.[114]
- The EU as a whole banned the use of medically important antibiotics for growth promotion and established an EU-wide AR monitoring system in 1999, then phased out all antibiotics use for growth promotion by 2006.[115] The prevalence of AR bacteria has subsequently declined in livestock, meat and people in the EU.[116]
- While not a member of the EU, Norway has considerable influence over EU aquaculture through companies like

Room for improvement

A number of organisations and companies adopt positions that appear supportive of a precautionary approach to antibiotic use in food-producing animals, but underlying policies and activities bring into question their commitment to a ban on all routine nontherapeutic uses. Food & Water Europe calls on them to make their support for such a ban clear.

The European Platform for the Responsible Use of Medicines in Animals (EPRUMA), which includes feed and drug manufacturers who profit from the sale of veterinary antibiotics, calls the preventative use of antibiotics where no disease has been diagnosed "a necessary part of disease management".[138]

While the Responsible Use of Medicines in Agriculture Alliance (RUMA), an associate member of EPRUMA, rightly points to a need for clear definitions, it also supports the use of antibiotics in animals "in order to prevent the occurrence of disease or infection".[139] RUMA "responsible use" guidance aims to "enable poultry producers to discontinue routine antimicrobial use"[140], but says, "Some bacterial infections are best dealt with by treatment before the clinical signs."[141] RUMA guidance for pigs advises, "Antimicrobials are sometimes used to treat a group of animals to prevent diseases that might occur.... Use for prevention is avoided whenever possible but may be necessary mainly during periods when stress is imposed on animals, e.g., changes in diet, weaning, transport and mixing."[142]

Industry responses to the Commission's draft Regulations support preventative use of antibiotics, so it is important for these organisations to clarify that this should not include treatment when no disease has been diagnosed. European farmers' representative Copa-Cogeca, said clearly, "[P]reventive use [of feed containing antibiotics] should be allowed".[143] Elsewhere Copa-Cogeca outlines the circumstances under which it calls preventative use "necessary".[144] The International Federation for Animal Health Europe, representing the animal health industry, also supports preventative group treatment of animals.[145]

While animals without visible symptoms may be infected and in need of treatment, Food & Water Europe supports the views of the Environment and Agriculture Committees that disease must be diagnosed before antibiotics are administered.

Marine Harvest, the world's largest producer of Atlantic salmon.[117] The O'Neill Report cites Norwegian Government figures of a 99 percent fall in antimicrobial use in aquaculture between 1987 and 2013 despite an increase in production, due to improved practices and stricter regulations.[118] The WHO says, "[I]mproved management of fish farms and the introduction of effective vaccines can significantly reduce the usage of antibiotics."[119] A 2009 study found that the antimicrobial sales for aquaculture in the UK have also declined, saying, "It has been suggested that this reduction is due mainly to improved husbandry techniques and the use of vaccines."[120]

It is clearly entirely possible to dramatically reduce antibiotic use in food-producing animals on land and at sea while maintaining or increasing production with improved animal husbandry backed up by tough enforcement of strict regulations. Eliminating all routine nontherapeutic use of antibiotics in food-producing animals is the next step.

Recommendations

The development and spread of AR bacteria are complex processes, and reversing them is difficult, if not impossible. There is no doubt that research and monitoring need to be improved to help identify, quantify and control the problem.

While the EU has gone some way towards improving how antibiotics are used, more needs to be done to eliminate routine nontherapeutic use of antibiotics in the rearing of our food animals in order to protect antibiotic efficacy for human and veterinary medicine.

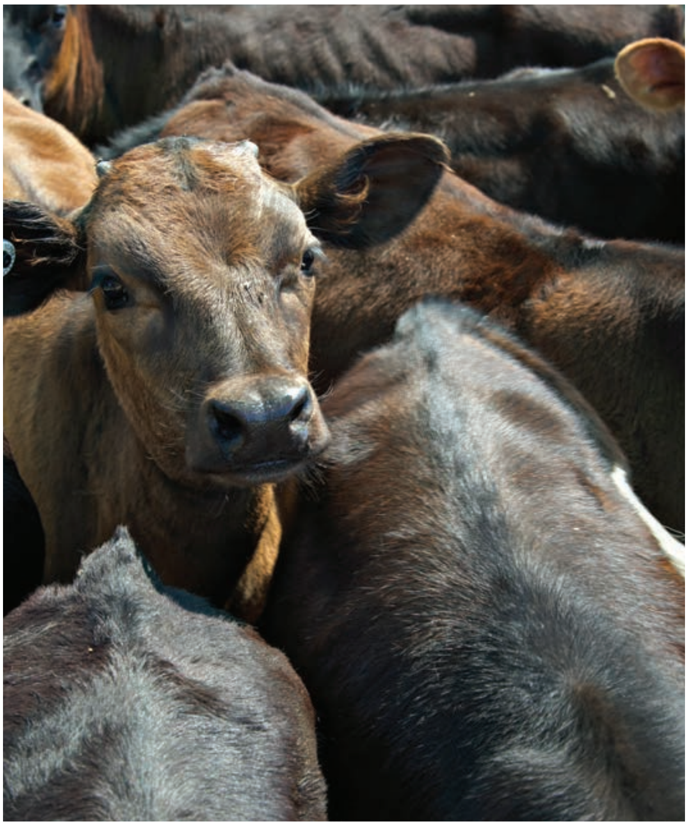
The European Union is currently considering two new Regulations that could be of critical help in this regard:

1. A comprehensive proposed Regulation on veterinary medicinal products (VMP) (2014/0257/COD).[121]
2. A proposed Regulation on the manufacture, placing on the market and use of medicated feed (2014/0255/COD).[122]

A number of important amendments from the Committee on Environment, Public Health and Food Safety[123] and the Committee on Agriculture[124] would, if adopted, explicitly ban the nontherapeutic use of antibiotics in food-producing animals via the VMP Regulation, which would then carry over into the implementation of the application of the medicinal feed Regulation.

Food & Water Europe considers it extremely important that the new Regulations include the amendments banning routine nontherapeutic use of antibiotics or others that do the same job. A ban is supported by the EMA.[125] It is also important, therefore, for Members of the European Parliament to ensure that no amendments are included in the new Regulations that water down a tough stance restricting antibiotic use.

Food & Water Europe also recommends that EU Member States be required to provide extension services to farmers to foster understanding of the need to restrict nontherapeutic antibiotic use, enable improved monitoring and reporting, and offer advice on alternative methods for controlling disease through improved animal husbandry and other on-farm practices.



Sadly, some vested interests may undermine the ban we need.

The problems became apparent very early in the process aiming to reform the law on veterinary medicinal products. In 2010, the Commission conducted a wide-ranging public consultation about reforming the laws regulating veterinary medicines that eventually informed the draft Regulations now under consideration. The pharmaceutical industry responded enthusiastically to the Commission's particular welcome to its input,[126] providing 35 of the 172 responses, pulling total business involvement up to 52 percent of submissions.[127]

The responses to one question are particularly revealing. When asked, "Would you favour that the legal framework provides a specific legal basis to restrict the use of antimicrobials which are critical for human medicine?", 51 percent of respondents answered that they did not.[128] This is disappointing. Such a restriction is not as far-reaching as a full ban on all nontherapeutic use of antibiotics, and, with clear implications for human health, supporting such a move would presumably fit squarely within any corporate social responsibility framework.

While the breakdown of respondents is outlined for other questions in the Commission's report of the consultation, the Commission did not reveal which sectors object to this suggestion. Due to the fact that some of the 32 anonymous responses reported on the Commission's website include pharmaceutical companies,[129] and the fact that the Commission states that it has neither published submissions from those requesting confidentiality nor included postal or email responses in its figures,[130] it is impossible to get a comprehensive picture of who is lobbying against a move that some consider vital to safeguarding antibiotic efficacy in human medicine.

However, an examination of the submissions that are available gives an indication of the sources of difficulty. The following pharmaceutical companies and associations are "not at all" in favour of restricting veterinary use of antimicrobials critical to human medicine[131]: Alpharma Animal Health, now part of the U.S. conglomerate Pfizer[132]; The Animal and Plant Health Association of Ireland; Bayer Animal Health; The Federation for Animal Health of Germany; European Group for Generic Veterinary Products; International Federation for Animal Health Europe; the association of manufacturers and importers of veterinary medicinal products of the Netherlands; Janssen Animal Health, now part of the U.S. conglomerate Eli Lilly[133]; National Office of Animal Health Ltd; Novartis Animal Health Inc, now part of U.S. conglomerate Eli Lilly[134]; Pfizer Animal Health, Veterinary Medicine R & D; the association of the French animal health industry; VIRBAC SA and five anonymous pharmaceutical companies.

By comparison, a number of public bodies "very much" support such a restriction, including[135]: the Italian Directorate General for animal health and veterinary drugs; the French authorities; the chemical safety office of the German Federal Environment Agency; the medical products agency of Sweden; and the Ministry of Agriculture and Forestry of Finland. In addition, a number of public bodies "clearly" favour such a restriction, including the Ministry of Agriculture, Nature and Food Quality of the Netherlands and the National Organization for Medicines of Greece.[136] Finally, the EMA Committee for Medicinal Products for Veterinary Use "clearly" favours a restriction, and the Pharmaceutical Group of the European Union favours a restriction "very much".[137]

The pharmaceutical industry lobbies MEPs against a mandatory ban on routine nontherapeutic use of antibiotics in animals in favour of a voluntary scheme. Food & Water Europe believes that this is effectively lobbying for the *status quo*.

The O'Neill Report found, "The majority of studies opposing a reduction of agricultural antimicrobial use were authored by people affiliated to either governments or industry," concluding, "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."[146]

Endnotes

1 Boucher, Helen et al. "Bad bugs, no drugs: No ESKAPE! An update from the Infectious Diseases Society of America." *Clinical Infectious Diseases.* Vol. 48, Iss. 1. 2009 at 1; The National Health Service. "The Antibiotics Awareness Campaign." Accessed at http://www.nhs.uk/nhsengland/arc/pages/aboutarc.aspx.

2 Public Health England (PHE). "Health Matters: Antimicrobial resistance." 10 December 2015. Accessed at https://www.gov.uk/government/publications/health-matters-antimicrobial-resistance/health-matters-antimicrobial-resistance.

3 *Ibid.*

4 Food and Agriculture Organization of the United Nations (FAO). Fisheries and Aquaculture Department. "Cultured Aquatic Species Information Programme: Dicentrarchus labrax." 2015. Accessed at http://www.fao.org/fishery/culturedspecies/Dicentrarchus_labrax/en.

5 Marshall, Bonnie and Stuart Levy. "Food animals and antimicrobials: impacts on human health." *Clinical Microbiology Reviews.* Vol. 24, Iss. 4. 2011; Silbergeld, Graham et al. "Industrial food animal production, antimicrobial resistance, and human health." *Annual Review of Public Health.* Vol. 29. 2008 at 158; U.S. Food and Drug Administration (FDA). National Antibiotic Resistance Monitoring System (NARMS). "2011 Retail Meat Report." 2013 at 6.

6 Silbergeld et al., 2008 at 151.

7 Johnson, James. University of Minnesota School of Medicine. Testimony on "The Science Is Clear: Inappropriate Use of Antibiotics in Animal Agriculture Threatens Public Health." Congressional Hearing sponsored by Center for Science in the Public Interest and Johns Hopkins University Center for a Livable Future. 8 March 2012.

8 Marshall and Levy, 2011 at 718.

9 Silbergeld et al., 2008 at 151; Meister, Karen. Supervisory Congressional Affairs Specialist. U.S. Department of Health and Human Services, U.S. Food and Drug Administration (FDA). Letter to Representative Louise Slaughter. 19 April 2011.

10 Marshall and Levy, 2011 at 718 to 719.

11 *Ibid.* at 719.

12 Silbergeld et al., 2008 at 151; Meister, 2011.

13 Marshall and Levy, 2011 at 719 and 726.

14 Gilchrist, M.J. et al. "The potential role of Concentrated Animal Feeding Operations in infectious disease epidemics and antibiotic resistance." *Environmental Health Perspectives.* Vol. 115, Iss. 2. 2007 at 313.

15 O'Neill, Jim (Chair, The Review on Antimicrobial Resistance). "Antimicrobials in Agriculture and the Environment: Reducing unnecessary use and waste." December 2015 at 5.

16 *Ibid.* at 5 and 7.

17 Office of Congresswoman Louise Slaughter. 13 May 2011; Meister, 2011.

18 FDA. Center for Veterinary Medicine (CVM). "2012 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals." September 2014 at 44.

19 PHE. "UK One Health Report: Joint report on human and animal antibiotic use, sales and resistance, 2013." July 2015 at 12.

20 O'Neill, 2015 at 7.

21 Rodgers, C.J. and M.D. Furones. "Antimicrobial agents in aquaculture: practice, needs and issues." In Rogers, C. and B. Basurco (eds.). "The use of veterinary drugs and vaccines in Mediterranean aquaculture." *Options Méditerranéennes: Série A. Séminaires Méditerranéens.* No. 86. 2009 at 48.

22 FAO, 2015.

23 Silbergeld et al., 2008 at 156; Smith, David L. et al. "Agricultural antibiotics and human health: Does antibiotic use in agriculture have a greater impact than hospital use?" *PLoS Medicine.* Vol. 2, Iss. 8. 2005 at 731.

24 Marshall and Levy, 2011 at 723.

25 Silbergeld et al., 2008 at 152.

26 Marshall, Bonnie et al. "Commensals: Underappreciated reservoirs of resistance." *Microbe.* May 2009 at 231.

27 *Ibid.*; Marshall and Levy, 2011 at 728.

28 Chen, J. et al. "Occurrence and persistence of erythromycin resistance genes (erm) and tetracycline resistance genes (tet) in waste treatment systems on swine farms." *Microbial Ecology.* Vol. 60, Iss. 3. 2010 at 480.

29 Chee-Sanford, J.C. et al. "Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste." *Journal of Environmental Quality.* Vol. 38. 2009 at 1086.

30 Marshall and Levy, 2011 at 727; Chee-Sanford et al., 2009 at 1094.

31 Chee-Sanford et al., 2009 at 1099.

32 Chen et al., 2010 at 479 to 480.

33 Furtula, V. et al. "Veterinary pharmaceuticals and antibiotic resistance of *Escherichia coli* isolates in poultry litter from commercial farms and controlled feeding trials." *Poultry Science.* Vol. 89. 2010 at 180.

34 Chee-Sanford et al., 2009 at 1088.

35 *Ibid.* at 1086.

36 Rule, A.M. et al. "Food animal transport: A potential source of community exposure to health hazards from industrial farming (CAFOs)." *Journal of Infection and Public Health.* Vol. 1, Iss. 1. 2008 at 37.

37 Graham, J.P. et al. "Antibiotic-resistant *Enterococci* and *Staphylococci* isolated from flies collected near confined poultry feeding operations." *Science of the Total Environment.* Vol. 407, Iss. 8. 2009 at 8.

38 Marshall and Levy, 2011 at 726.

39 Looft, Torey et al. "In-feed antibiotic effects on the swine intestinal microbiome." *Proceedings of the National Academy of Sciences.* Vol. 109, Iss. 3. 17 January 2012 at 1.

40 *Ibid.* at 4.

41 Gibbs S.E. et al. "Isolation of antibiotic-resistant bacteria from the air plume downwind of a swine confined or Concentrated Animal Feeding Operation." *Environmental Health Perspectives.* Vol. 114, Iss. 7. 2006 at 1032.

42 European Centre for Disease Prevention and Control, European Food Safety Authority and European Medicines Agency (ECDC/EFSA/EMA). "ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals." 30 January 2015 at 58.

43 Silbergeld et al., 2008 at 159.

44 Levy, S.B. et al. "Changes in intestinal flora of farm personnel after introduction of a tetracycline-supplemented feed on a farm." *New England Journal of Medicine*. Vol. 295. 1976 at 583.

45 Gilchrist et al., 2007 at 314.

46 Price, L.B. et al. "Elevated risk of carrying gentamicin-resistant *Escherichia coli* among U.S. poultry workers." *Environmental Health Perspectives*. Vol. 115. 2007 at 1738 and 1740.

47 Khanna, T. et al. "Methicillin-resistant S*taphylococcus aureus* colonization in pigs and pig farmers." *Veterinary Microbiology*. Vol. 128. 2008 at 298; Fey, Paul et al. "Ceftriaxone-resistant *Salmonella* infection acquired by a child from cattle." *New England Journal of Medicine*. Vol. 342, Iss. 17. 27 April 2000 at 1242.

48 Kluytmans, J.A. "Methicillin-resistant *Staphylococcus aureus* in food products: Cause for concern or complacency?" *Clinical Microbiology and Infection*. Vol. 16, Iss. 1. 2010 at 11.

49 Smith, Tara et al. "Methicillin-resistant *Staphylococcus aureus* in pigs and farm workers on conventional and antibiotic-free swine farms in the USA." *PLOS ONE*. Vol. 8, Iss. 5. May 2013 at e63704; Rinsky, Jessica et al. "Livestock-associated methicillin and multidrug resistant *Staphylococcus aureus* is present among industrial, not antibiotic-free livestock operation workers in North Carolina." *PLOS ONE*. Vol. 8, Iss. 7. July 2013 at 6.

50 Casey, Joan et al. "High-density livestock operations, crop field application of manure, and risk of community-associated methicillin-resistant *Staphylococcus aureus* infection in Pennsylvania." *JAMA Internal Medicine*. Vol. 173, Iss. 21. 25 November 2013.

51 Translational Genomics Research Institute. [Press release]. "TGen-led study suggests origins of MRSA strain in food animals." 21 February 2012.

52 Price, Lance et al. "*Staphylococcus aureus* CC398: Host adaptation and emergence of methicillin resistance in livestock." *mBio*. Vol. 3, Iss. 1. January/February 2012 at 1.

53 Cogliani, Carol et al. "Restricting antimicrobial use in food animals: Lessons from Europe." *Microbe*. Vol. 6, Iss. 6. 2011 at 274 to 275.

54 Smith et al., 2005 at 733.

55 O'Neill, 2015 at 10.

56 World Health Organization, Europe Regional Office (WHO Europe). "Tackling antibiotic resistance from a food safety perspective in Europe." 2011 at 13.

57 ECDC/EFSA/EMA, 2015 at 97.

58 *Ibid.* at 58; WHO Europe, 2011 at xiii.

59 Smith et al., 2005 at 732.

60 *Ibid.* at 732.

61 Johnson, 2012.

62 Gilchrist et al., 2007 at 313.

63 European Centre for Disease Prevention and Control and the European Medical Association. [Joint press release.] "The bacterial challenge – time to react. A call to narrow the gap between multidrug-resistant bacteria in the EU and development of new antibacterial agents." 17 September 2009.

64 European Commission. "Antimicrobial resistance." 14 December 2015. Accessed at http://ec.europa.eu/dgs/health_food-safety/amr/index_en.htm.

65 PHE, July 2015 at 10.

66 National Institute for Care and Health Excellence (NICE). "British National Formulary: Ciproflaxacin." Accessed at http://www.evidence.nhs.uk/formulary/bnf/current/5-infections/51-antibacterial-drugs/5112-quinolones/ciprofloxacin.

67 NICE. "British National Formulary: Cefotaxime." Accessed at http://www.evidence.nhs.uk/formulary/bnf/current/5-infections/51-antibacterial-drugs/512-cephalosporins-carbapenems-and-other-beta-lactams/5121-cephalosporins/cefotaxime.

68 NICE. "British National Formulary: Ceftazidime." Accessed at http://www.evidence.nhs.uk/formulary/bnf/current/5-infections/51-antibacterial-drugs/512-cephalosporins-carbapenems-and-other-beta-lactams/5121-cephalosporins/ceftazidime.

69 PHE, July 2015 at 22.

70 *Ibid.* at 22.

71 *Ibid.* at 11.

72 NICE. "British National Formulary: Erythromycin." Accessed at http://www.evidence.nhs.uk/formulary/bnf/current/5-infections/51-antibacterial-drugs/515-macrolides/erythromycin.

73 PHE, July 2015 at 11.

74 Department for Environment, Health and Rural Affairs and Public Health England. "Zoonoses Summary Report: UK 2014." December 2015 at 3.

75 U.S. Centers for Disease Control and Prevention (CDC). "Antibiotic Resistance in the United States, 2013." 2013 at 6.

76 Food & Water Watch analysis of CDC, 2013; Murphy, Joan. "CDC calls for phase out for growth promoters." *Food Chemical News*. 17 September 2013.

77 Koyama, Y. et al. "A new antibiotic 'colistin' produced by spore-forming soil bacteria." *Journal of Antibiotics*. Vol. 3. 1950 at 457 to 458.

78 Timmerman, T. et al. "Quantification and evaluation of antimicrobial drug use in group treatments for fattening pigs in Belgium." *Preventive Veterinary Medicine*. Vol. 74. 2006 at 251 to 263.

79 Nord, N.M. and P.D. Hoeprich. "Polymyxin B and Colistin. A Critical Comparison." *New England Journal of Medicine*. Vol. 270. 1964 at 1030 to 1035.

80 European Medicines Agency (EMA). "Use of colistin products in animals within the European Union: Development of resistance and possible impact on human and animal health." 19 July 2013 at 10.

81 *Ibid.* at 3.

82 *Ibid.* at 7.

83 "UK's first colistin-based antimicrobial for poultry." *Vet Times*. 28 July 2010.

84 EMA, July 2013 at 4.

85 PHE. "First detection of plasmid-mediated colistin resistance (*mcr*-1 gene) in food and human isolates in England and Wales." 7 December 2015. Gallagher, James. "Bacteria that resist 'last antibiotic' found in UK." *BBC*. 21 December 2015.

86 Advisory Committee on Animal Feedingstuffs. "Minutes of the Sixty-second Meeting of ACAF Held on 9 October 2013."

87 Liu, Y. et al. "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*. Published online 18 November 2015.

88 "Why we need greater political action against the overuse of antibiotics in agriculture." *The Times*. 22 November 2015.

89 Driver, Alistair. "Vets calls for proportionate response to Chinese antibiotic resistance findings." *Farmers' Guardian Insight*. 26 November 2015.

90 UK Parliament. "Veterinary Medicine: Antibiotics: Written question – 18674." 11 December 2015.

91 Responsible Use of Medicines in Agriculture Alliance (RUMA). [Press release.] "RUMA announces voluntary restrictions on colistin use in UK livestock." 4 December 2015.

92 British Society for Antimicrobial Chemotherapy. [Press release]. "Discovery of colistin-resistant bacteria in Denmark: BSAC and Antibiotic Action respond." Undated response to a media story on 4 December 2015.

93 EMA. [Press release]. "Committee for Medicinal Products for Veterinary Use (CVMP) meeting of 8-10 December 2015." 11 December 2015.

94 Woodmansey, David. "Scientists find mcr-1 gene in food and human isolates." *Vet Times*. 11 December 2015.

95 Knapton, Sarah. "Antibiotic resistant E.coli is circulating in Britain, warn public health officials." *The Telegraph*. 21 December 2015.

96 PHE, 7 December 2015.

97 *Ibid.*

98 Gallagher, 21 December 2015.

99 Interview, BBC Radio 4 *Today*, 22 December 2015.

100 *Ibid.*

101 Smith, David et al. "Animal antibiotic use has an early but important impact on the emergence of antibiotic resistance in human commensal bacteria." *Proceedings of the National Academy of Sciences*. Vol. 99, Iss. 9. 30 April 2002 at 6434 and 6439.

102 Marshall and Levy, 2011 at 722; Silbergeld et al., 2008 at 156 to 157.

103 *See:* Sorum, M. et al. "Prevalence, persistence, and molecular characterization of glycopeptide-resistant enterococci in Norwegian poultry and poultry farmers 3 to 8 years after the ban on avoparcin." *Applied Environmental Microbiology*. Vol. 72. 2006 at 516 to 521; Silbergeld et al., 2008 at 157.

104 Marshall and Levy, 2011 at 722.

105 Animal Health Institute (AHI). [Press release]. "AHI comment on PCAST report on antibiotic resistance." 18 September 2014; AHI. [Press release]. "AHI statement on CDC report." 16 September 2013; National Pork Producers Council and American Meat Institute. "Groups Respond to White House Executive Order on Antibiotic Resistance." *National Hog Farmer*. 18 September 2014.

106 RUMA. [Press release.] "RUMA promotes 'as little as possible, but as much as necessary' antibiotic use, for the good of animal health and welfare." 30 March 2009.

107 Pruden, Amy et al. "Management options for reducing the release of antibiotics and antibiotic resistance genes to the environment." *Environmental Health Perspectives*. Vol. 121, Iss. 8. August 2013 at 879.

108 Levy, Sharon. "Reduced antibiotic use in livestock: How Denmark tackled resistance." *Environmental Health Perspectives*. Vol. 122, Iss. 6. June 2014 at A162.

109 Cogliani et al., 2011 at 274 to 276.

110 Aestrup, Frank et al. "Changes in the use of antimicrobials and the effects on productivity of swine farms in Denmark." *American Journal of Veterinary Research*. Vol. 71, Iss. 7. July 2010 at 730.

111 *Ibid.* at 726 and 730.

112 Levy, June 2014 at A162.

113 Mevius, Dik and Dick Heederik. "Reduction of antibiotic use in animals. 'Let's go Dutch.'" *Journal of Consumer Protection and Food Safety*. Vol. 9. 2014 at 179; Levy, June 2014 at A164.

114 Netherlands National Institute for Public Health and the Environment. "Antibiotic resistance no longer increasing but vigilance remains necessary." 26 June 2014. On file at Food & Water Watch and accessed at http://www.rivm.nl/en/Documents_and_publications/Common_and_Present/Newsmessages/2014/Antibiotic_

resistance_no_longer_increasing_but_vigilance_remains_necessary; Mevius and Heederik, 2014 at 180.

115 Cogliani et al., 2011 at 275.

116 Smith et al., 2005 at 731.

117 Marine Harvest. "In brief." Undated. Accessed at http://www.marineharvest.com/about/in-brief/.

118 O'Neill, 2015 at 7.

119 WHO Europe, 2011 at xiv.

120 Rodgers and Furones, 2009 at 54.

121 European Commission (EC). "Proposal for a Regulation of the European Parliament and of the Council on veterinary medicinal products." 10 September 2014.

122 EC. "Proposal for a Regulation of the European Parliament and of the Council on the manufacture, placing on the market and use of medicated feed and repealing Council Directive 90/167/EEC." 10 September 2014.

123 European Parliament Committee on the Environment, Public Health and Food Safety. "Draft Report on the proposal for a regulation of the European Parliament and of the Council on veterinary medicinal products." 2014/0257(COD). 14 April 2015 at 78 and Amendment 97.

124 European Parliament Committee on Agriculture and Rural Development. "Opinion of the Committee on Agriculture and Rural Development on the proposal for a regulation of the European Parliament and of the Council on veterinary medicinal products." 2014/0257(COD). 23 July 2015 at 3, 4 and Amendments 80, 144,149, 151, 153, 158 and 169.

125 EMA. "Question and answer on the CVMP guideline on the SPC for antimicrobial products (EMEA/CVMP/SAGAM/383441/2005)." 9 October 2014.

126 EC. "Report on the European Commission's public online consultation." 2011 at 25. Accessed at http://ec.europa.eu/health/files/veterinary/vet_pubcons_rep2011.pdf.

127 EC, 2011 at 2.

128 *Ibid.* at 10 and 11.

129 EC. "Revision of the legal framework for veterinary medicinal products - Responses of stakeholders." Undated. Accessed at http://ec.europa.eu/health/veterinary-use/pubcons_frame_index_en.htm.

130 EC, 2011 at 1.

131 EC. "Revision of the legal framework for veterinary medicinal products – Responses of stakeholders." Undated. Response from Alpharma Animal Health. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_alpharma_animal_health_149_en.pdf; Response from The Animal and Plant Health Association of Ireland. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_animal_and_plant_health_association_ireland_107_en.pdf; Response from Bayer Animal Health. Accessed at http://ec.europa.eu/health/files/veterinary/revision2/vet_bayer_en.pdf; Response from The Federation for Animal Health of Germany. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_bundesverband_fur_tiergesundheit_162_en.pdf; Response from European Group for Generic Veterinary Products (EGGVP). Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_eggvp__european_group_for_generic_veterinary_products__27_en.pdf; Response from International Federation for Animal Health Europe. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_ifah_europe_70_en.pdf; Response from the association of manufacturers and importers of veterinary medicinal products of the Netherlands. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_fidin_69_en.pdf; Response from Janssen Animal Health. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_janssen_animal_health_40_en.pdf; Response from National Office of Animal Health Ltd. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_national_office_of_animal_health_ltd_98_en.pdf; Response from Novartis Animal Health Inc. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_novartis_animal_health_inc__110_en.pdf; Response from Pfizer Animal Health, Veterinary Medicine R & D. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_pfizer_animal_health__veterinary_medicine_r___d_119_en.pdf; Response from The association of the French animal health industry. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_simv_33_en.pdf; Response from VIRBAC SA. Accessed at http://ec.europa.eu/health/files/veterinary/revision2/vet_virbar_en.pdf; Anonymous responses. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_unspecified_contact_information__101_en.pdf, http://ec.europa.eu/health/files/veterinary/revision/vet_unspecified_contact_information__102_en.pdf, http://ec.europa.eu/health/files/veterinary/revision/vet_unspecified_contact_information__35_en.pdf, http://ec.europa.eu/health/files/veterinary/revision/vet_unspecified_contact_information__39_en.pdf, http://ec.europa.eu/health/files/veterinary/revision/vet_unspecified_contact_information__79_en.pdf.

132 Zoetis. [Press release]. "Pfizer Animal Health begins integration with Alpharma." 2 March 2011. Accessed at https://www.zoetisus.com/news-and-media/pfizer-animal-health-begins-integration-with-alpharma.aspx.

133 Elanco. "The Elanco Story." Undated. Accessed via http://divvy.cantaloupe.tv/storybooks/63d31120-4a61-4fca-8dbd-41f33035d301/episode/1. Information quoted accessed at http://divvy.cantaloupe.tv/storybooks/63d31120-4a61-4fca-8dbd-41f33035d301/episode/2.

134 *Ibid.*

135 EC. "Revision of the legal framework for veterinary medicinal products - Responses of stakeholders." Undated. Response from the Italian Directorate General for animal health and veterinary drugs. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_ministero_della_slute_direzione_generale_sanita_animale_e_farmaco_veterinario_36_en.pdf; Response from the French authorities. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_french_authorities__85_en.pdf; Response from the chemical safety office of the German Federal Environment Agency. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_chemical_safety_german_federal_environment_agency__umweltbundesamt__75_en.pdf; Response from the medical products agency of Sweden. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_medical_products_agency___sweden_156_en.pdf; Response from the Ministry of Agriculture and Forestry of Finland. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_ministry_of_agriculture_and_forestry___finland_157_en.pdf.

136 EC. "Revision of the legal framework for veterinary medicinal products - Responses of stakeholders." Undated. Response from the Ministry of Agriculture, Nature and Food Quality of the Netherlands. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_ministry_of_agriculture__nature_and_food_quality___the_netherlands_10_en.pdf; Response from the National Organization for Medicines of Greece. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_national_organization_for_medicines_eof____greece_158_en.pdf.

137 EC. "Revision of the legal framework for veterinary medicinal products - Responses of stakeholders." Undated. Response from EMA Committee for Medicinal Products for Veterinary Use. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_committee_for_medicinal_products_for_veterinary_use__cvmp____european_medicines_agency_13_en.pdf; Response from the Pharmaceutical Group of the European Union. Accessed at http://ec.europa.eu/health/files/veterinary/revision/vet_the_pharmaceutical_group_of_the_european_union__pgeu__125_en.pdf.

138 European Platform for the Responsible Use of Medicines in Animals. "Best-practice framework for the use of antibiotics in food-producing animals in the EU." 2015 at 18.

139 RUMA. "RUMA Position Statement on the Preventative Use of Antibiotics in Farm Animals." 2013 at 2.

140 RUMA. "Responsible use of antimicrobials in poultry production." 2005 at 5.

141 *Ibid.* at 7.

142 RUMA. "Responsible use of antimicrobials in pig production." 2013 at 28 and 29.

143 Copa-Cogeca. "COPA-COGECA reaction to the Commission's proposal for a Regulation of the Euroepan Parlieament and of the Council on veterinary medicinal products and to the Commission's proposal for a Regulation of the European Parliament and of the Council on the manufacture, placing on the market and use of medicated feed repealing Directive 90/157/EEC." 6 February 2015 at 8.

144 Copa-Cogeca. "The responsible use of antimicrobials in food-producing animals: Copa-Cogeca's views." 20 April 2012 at 3.

145 International Federation for Animal Health Europe. "Position paper: Proposal for a Regulation on the manufacture, placing on the market and use of medicated feed." Undated. Accessed at http://www.ifaheurope.org/ifah-media/position-papers/251-position-paper-proposal-for-a-regulation-on-the-manufacture,-placing-on-the-market-and-use-of-medicated-feed-com-2014-556.html.

146 O'Neill, 2015 at 10.

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