

# Antimicrobial Resistance One Health Colloquium

18–19 December 2014

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## Introduction

This document provides a summary of proceedings at the Antimicrobial Resistance (AMR) One Health Colloquium hosted by the Centre on Global Health Security at Chatham House on 18–19 December 2014. The event focused on deepening understanding of how to address the issues at the animal–human interface that contribute to establishing and further reinforcing AMR as a worldwide public health concern.

More specifically, the colloquium aimed to examine the direct and indirect benefits and risks to human health from livestock, including the impact on the growing problem of AMR, and strategies for addressing this.

The proceedings were designed to encourage discussion between representatives of different sectors and disciplines, in line with the principles behind the global One Health Initiative.

Participants included experts from the animal and human health sectors, trade and commerce, governments, and international organizations such as the World Health Organization (WHO), the UN Food and Agriculture Organization (FAO), the World Organisation for Animal Health (OIE) and the World Bank. Attendance was by invitation only, and the meeting was held under the Chatham House Rule.<sup>1</sup>

The core issues addressed on the first day of the event concerned fostering cross-sector efforts to combat AMR, and how collaborative partnerships can be developed in line with the One Health Initiative. The second day focused on presentations offering insight into several important issues that can guide strategies to combat AMR, including animal welfare, reforming livestock husbandry practices, and vaccine development. In addition, the meeting aimed to enable greater insight into how partnerships including the Livestock Global Alliance (LGA) and the Global Agenda for Sustainable Livestock (GASL) can work to reduce AMR by tackling relevant issues at the animal–human interface.

## Background

It is widely accepted that AMR – resistance to drug treatments exerted by microbial agents of disease, including bacteria, viruses, fungi and parasites – is a serious threat to global health security.<sup>2</sup> This is not least because resistance transcends borders and threatens the scientific advancements that have been made in treating a wide range of diseases. Furthermore, those infected with an antimicrobial-resistant pathogen remain infectious for longer periods of time, increasing the opportunity for resistant infection to be spread to others.<sup>3</sup>

Discourse on AMR has framed the problem as an urgent threat. This is in part due to a widely repeated claim by WHO Director-General Dr Margaret Chan that ‘the end of modern medicine as we know it’ is on the horizon should we be unable to turn the tide of AMR, and that we could then live in a world in which antimicrobial drugs are no longer a viable part of the arsenal against the threat of diseases.<sup>4</sup>

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<sup>1</sup> When a meeting, or part thereof, is held under the Chatham House Rule, participants are free to use the information received, but neither the identity nor the affiliation of the speaker(s), nor that of any other participant, may be revealed.

<sup>2</sup> World Health Organization. *Antimicrobial Resistance*. WHO. Fact sheet no. 194, 2012. [Online] Available from: <http://www.who.int/mediacentre/factsheets/fs194/en/> [Accessed 19 February 2015].

<sup>3</sup> Heymann, DL. Resistance to Anti-Infective Drugs And the Threat to Public Health. *Cell*. 2006; 124(4): 671-5.

<sup>4</sup> Chan M. (2012). *Antimicrobial resistance in the European Union and the world*. [Keynote address] Conference on Combating antimicrobial resistance: time for action. Copenhagen. 14 March 2012. [Online] Available from: [http://www.who.int/dg/speeches/2012/amr\\_20120314/en/](http://www.who.int/dg/speeches/2012/amr_20120314/en/) [Accessed 24 February 2015].

The gravity of this issue ultimately lies in the fact that should antibiotics and other drugs designed to target infectious agents stop working, medical interventions that are now routine could become high-risk. Among others, caesarean sections, hip-replacement surgeries and the treatment of urinary tract infections all rely on antibiotics either for treatment or for prevention of infection. Modern medicine, at least in the developed world, is well equipped and easily able to treat such conditions, but only because of the availability of effective antimicrobial drugs. It is feared that health care systems would essentially buckle without them.

One of the most fundamental aspects of AMR is the strong association it has with modern livestock-rearing. Considering the use of antibiotics alone, it has been reported that in the United States 84 per cent of all antibiotics are used in agriculture,<sup>5</sup> with the majority being used in livestock-rearing. While there is no comprehensive breakdown illustrating the extent of antimicrobial use in livestock in terms of its purpose, it is believed that they are mostly used in this sector to achieve non-therapeutic gains, such as growth.<sup>6</sup> Antimicrobial use in livestock compounds the AMR problem, given that use in the sector is considered to be the primary cause of resistance developing in some pathogens that infect humans.<sup>7</sup> Moreover, the use of antimicrobials within the livestock industry has garnered considerable attention from a variety of stakeholders since it can be highly detrimental to animal welfare, partly because it reduces the effectiveness of drugs targeted at treating infection in animals.

There are several incentives to use antimicrobials as growth promoters in modern commercial farming. For instance, introducing antimicrobial drugs into animal feed allows more energy and resources to be directed towards growth. This clearly produces an incentive for farmers to use antimicrobials as a prophylactic measure, as livestock with higher growth rates are more commercially viable. Intensive farming practices are known to create unsanitary environments that facilitate the spread of infection and consequently inhibit the growth of livestock – poultry in particular. Thus, antimicrobial use offers farmers practising intensive animal-rearing (which often involves the containment of herds in tightly confined spaces) the potential to maintain growth in animals despite conditions that promote infection and disease.

Given the interconnected interests of those working across several sectors, including human health, veterinary medicine and the environment, a One Health Initiative to improve the health of humans and animals has been developed.<sup>8</sup> The One Health Initiative is considered to be an important framework for addressing several issues threatening health, including AMR. The essence of the One Health approach to tackling AMR is in the understanding that in order to combat AMR appropriately and effectively, concerted collaborative efforts are necessary across the human health, veterinary medicine and environment sectors. Equally important is the recognition that the One Health approach must involve partnerships between those working at the interface of multiple related disciplines. The One Health approach is based on the premise that leveraging the insight and capacity of veterinarians, physicians and epidemiologists, as well as researchers in public health and ecology, is crucial to ensuring a robust response to the threat of AMR.

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<sup>5</sup> Harris G. Antibiotics in Animals Need Limits, F.D.A. Says. *New York Times*, 28 June 2010. [Online] Available from: [http://www.nytimes.com/2010/06/29/health/policy/29fda.html?\\_r=1](http://www.nytimes.com/2010/06/29/health/policy/29fda.html?_r=1) [Accessed 23 February 2015].

<sup>6</sup> Mellon M, Benbrook, C and Benbrook, KL. *Hogging it!: Estimates of antimicrobial abuse in livestock*. Union of Concerned Scientists. 2001. [Online] Available from: [http://www.ucsusa.org/food\\_and\\_agriculture/our-failing-food-system/industrial-agriculture/hogging-it-estimates-of.html#.VRAxzOEZYtF](http://www.ucsusa.org/food_and_agriculture/our-failing-food-system/industrial-agriculture/hogging-it-estimates-of.html#.VRAxzOEZYtF) [Accessed 24 February 2015].

<sup>7</sup> Alliance to Save Our Antibiotics. *Antimicrobial Resistance – Why the Irresponsible Use of Antibiotics In Agriculture Must Stop*. Alliance to Save Our Antibiotics, 2014. [Online] Available from: [www.sustainweb.org/publications/antimicrobial\\_resistance/](http://www.sustainweb.org/publications/antimicrobial_resistance/) [Accessed 24 February 2015].

<sup>8</sup> <https://www.avma.org/kb/resources/reference/pages/one-health.aspx>.

Greater dependence on animal food products and fundamental changes in land use have increased several global health risks, including the threat of emerging infectious diseases and heightened AMR. Responding to these threats requires a more unified strategy, which the One Health approach seeks to provide. Importantly, ensuring that action on AMR extends beyond the local and national level is a central element of the One Health approach. This is based on the belief that placing decision-making around AMR at the global level will foster political will, and on the understanding that reaching consensus under the One Health approach depends on political commitment.

### Key discussion themes

#### **The lack of understanding between the animal and human health sectors**

The discussion began with participants describing a pressing need to strengthen partnerships between those working in animal health and those working in human health. One participant argued that without more dynamic collaboration, the potential number of deaths due to AMR in humans could rise into the tens of millions, with the greatest proportion of those deaths occurring in the developing world. It was also noted that the lack of understanding between the two areas is in large part because of a lack of evidence underpinning the clinical guidelines used in both sectors. Improving mutual understanding was said to be as important as the need to advance understanding of how antibiotic use in animals affects human health.

It was noted that blaming individual institutions or specific sectors for AMR is not useful for advancing understanding or for promoting partnerships that will better tackle the problem. One participant pointed out that efforts should instead be focused on preventive measures that would make developing cures for infections caused by resistant pathogens no longer necessary. It was also argued that antibiotic use should be restricted to therapy; and that vaccines and good biosecurity, rather than antimicrobial drugs, should be used to prevent disease.

One participant emphasized that it is essential to acknowledge that the rate of antibiotic prescription for humans is extremely high in certain regions of the world, and that this is compounding the worrying rates of AMR globally. Stakeholders should prioritize reducing the overall amount of antibiotics used both in animals and humans, rather than focus on how to reduce the amount prescribed in one group and not the other. Likewise, many participants identified preventive measures, including vaccines, as being good areas for stakeholders to consider.

Improving research at every level from clinical analysis to the burden of AMR in different geographical areas was highlighted as another key concern, given that more understanding across the board will advance efforts to reduce the emergence and spread of resistant strains.

One participant pointed out that the debates around AMR among those working in animal health and human health have been contentious in the past; and that in order to advance efforts to overcome AMR, consensus on divisive issues will need to be reached.

Discussions also focused on the lack of understanding among the general public regarding the process of food production. One participant argued that this is a crucial factor in the low coverage generally given to AMR in the media, as it tends not to be seen by news editors as a viable and commercially popular topic.

## Prospects for the antibiotics pipeline and antibiotic alternatives

The focus of the discussion moved towards assessing the commercial opportunities for antibiotic alternatives and the regulatory hurdles preventing such products from entering the market. One participant noted that antimicrobial peptides have yet to be considered as having high market potential. Two other participants underlined the need for more antibiotic options in modern medicine: it was said that the pharmaceutical industry is allocating considerable resources to developing cancer drugs that will have the side effect of giving rise to more infections, thus creating the need to use more antibiotics.

A key point raised was that there has long been reluctance on the part of investors to fund the development of antibiotics, in part because regulators including the US Food and Drug Administration (FDA) and the European Medicines Agency have hurdles in respect of proving safety of antibiotics that are so high that it makes the cost of developing antibiotics unattractive to investors. However, it was also noted that this has created a gap in the market that some investors consider appealing.

The veterinary vaccine market has been growing by more than 4 per cent annually, according to projections shown by one participant, who referred to reports indicating that the veterinary medicines market could be worth \$8.6 billion in the near future. The drivers of this growth were discussed and several theories were put forward, such as greater demand for animal products worldwide having created, in turn, a greater demand for prophylaxis, including vaccines, in livestock.

The example was given of the Jenner Institute at the University of Oxford, where a partnership model has been established between vaccine developers with expertise in the human health and animal health sectors. This model was said to have been successful in advancing knowledge on vaccines targeted at diseases that have human–veterinary synergies, and that partnerships such as this have the potential to contribute significantly to efforts to overcome AMR.

One participant stated that the veterinary vaccine market will continue to grow, and that health and food security concerns, drug resistance and emerging diseases will be primary factors driving this growth.

## Spreading good practice

Several participants raised the issue of spreading good practice, with many discussing specific policy interventions to illustrate how AMR can be tackled in livestock.

One participant highlighted how in the Netherlands the authorities launched an AMR awareness-raising campaign targeting farmers after an outbreak of Q fever was traced to exposure to infected goat herds and after the first reported human death from an antibiotic-resistant urinary tract infection. The campaign was considered a key element in changing veterinary and farming practices. It was noted that policy-makers in the Netherlands prioritized recording the amount of antibiotics used on farms and required farmers to verify that first-line antibiotics had failed before they were allowed to use second- and third-line options. It was stated that because of the quality of the data it has amassed, the Netherlands is now at a stage where it is able to study the relationship between the use of antibiotics and resistance. However, one participant noted that the data collection and processing system in the Netherlands differs from that of other European states, and that it is not therefore possible to make accurate farm-level comparisons across the continent using these results.

Discussion later turned to the focus that policy-makers and regulators in the United States are giving to AMR. It was stated that the use of antimicrobial drugs in the United States has historically been

somewhat indiscriminate and inappropriate, in both humans and animals. One participant noted that an executive order issued by President Barack Obama on combating antibiotic resistance provided the foundation for the creation of a new National Strategy for Combating Antibiotic-Resistant Bacteria. It was also stated that the US government is adopting a One Health approach to AMR by building a multifaceted plan based on coordination between the human health, animal health and environment sectors. It was reported that the FDA is now targeting more strongly the non-judicious use of antimicrobial drugs in livestock, and that closer attention is being paid to eliminating the use of such drugs as growth promoters.

It was also noted that the United States is shifting towards increasing the responsibility of veterinarians for overseeing the therapeutic use of antimicrobial drugs in animals. One participant argued that the US policy of not outlawing the use of such drugs in food-producing animals is more successful than a ban, since the latter approach would require the presentation of a lengthy scientific rationale for each specific embargo pertaining to each individual drug. It was highlighted that the current method can be considered a success, since all pharmaceutical companies that produce antimicrobials for food-producing animals have complied with the FDA's advice voluntarily to phase out the use of these drugs.

One participant stated that US policy-makers should prioritize setting up appropriate strategies to ensure that the management of animal health is optimized, and that this, in turn, would support the management of human health. Another argued it is fundamentally important for the FDA to focus on tackling the routine preventive use of antibiotics, since this currently contributes strongly to the prevalence of AMR and is likely to supplant much of the growth-promoting use.

The role of innovation was discussed, and how technology can support the development of best practice around strategies to combat AMR in humans and animals. One participant set out the need for farming practices to become much more efficient in light of the risk of future food crises, and argued that it is essential to harness the potential offered by technology and innovation in order to realize these greater efficiencies. Another acknowledged that this is a key point, but establishing best practice also hinges on the creation of joint health systems linking animal and human health.

According to several participants, the close living proximity of humans and animals – especially livestock and pets – is reflected in how closely related drug-resistant pathogens in both groups are. Thus, it was argued strongly that breaking the barriers between the systems that separately regulate and manage human health and animal health will improve the ability to overcome the shared problem of AMR.

### **Animal welfare**

Another topic of discussion related to how best practice can affect animal welfare.

One participant pointed to recent FAO estimates indicating that livestock production will need to double in order to meet growing demand for animal products. The same participant also mentioned that accelerating livestock production in line with these greater demands risks eroding standards of animal welfare, which consequently could amplify the spread of AMR in animals and humans. Two breaches of animal welfare standards most likely to arise from these trends were said to be the confinement of animals in overly restrictive conditions, and the suffering that animals endure when high production levels are imposed.

It was emphasized that animal welfare has been adversely affected by the widespread use of antimicrobial drugs. Specific examples were referred to, including how the regular use of antibiotics in cows gives rise to mastitis, since using antibiotics in this way facilitates the housing of cattle in unhygienic conditions. One

participant mentioned that systems that permit the regular use of antibiotics inherently permit abuse of animal welfare standards, since they support practices including overcrowding and promote conditions that facilitate the spread of pathogens, therefore compounding AMR.

### **Building international capacity to tackle AMR more efficiently**

The theme of global collaboration between actors working in animal health, human health and environment sectors continued, with discussions around this shifting towards ways in which multilateral institutions can play a uniquely important role in the effort to overcome AMR.

One participant described the case of the World Bank, which was said to have been successful in streamlining the work of its agricultural and health programmes in response to the threat posed by avian influenza. It was stated that the World Bank is again engaging these two programmes with regard to combating AMR in animals and humans. The World Bank was also identified as playing an important role in contributing to general understanding of the impact of AMR on global trade, public health and economic growth; it has commissioned a report investigating the economic impact that would be likely to result from taking no action against AMR. The same participant also highlighted the importance of strengthening both national public health systems and veterinary systems, arguing that these must be robust enough to function well independently before they can engage in effective collaborative partnerships. The OIE, WHO, FAO and the World Bank were said to be involved in developing country assessment tools that are designed to strengthen these systems at the country level. It was also mentioned that these multilateral organizations are working together to create an operational framework that will guide developing countries in enhancing the ways in which these systems operate at the animal–human interface.

To illustrate how the private sector can contribute to enhancing domestic capacity to combat livestock disease that may be resistant to antimicrobial drugs, one participant cited the example of Somaliland. Two bans on livestock imports imposed by Saudi Arabia on Somaliland in the early 2000s, following outbreaks of Rift Valley Fever, triggered several adverse socio-economic effects there, reportedly including rises in rates of crime and poverty, and increased barriers to education. While the bans were in force, the Somaliland authorities were said not to have been able to demonstrate that the quality and health of the territory's livestock met trade standards set by Saudi Arabia. This resulted in private companies from the Gulf region investing in joint venture programmes with local Somaliland enterprises to build quarantine holding facilities, with the aim of ensuring the health of livestock. These efforts were said to have been responsible for the eventual reopening of livestock trade channels between Somaliland and Saudi Arabia.

The importance of developing countries having adequate capacity was mentioned again later in the discussions, in the context of such countries being at potential risk of suffering most from an increase in AMR.

Another participant highlighted the work of the European Union (EU) in conducting audits that investigate the extent to which its member states are ensuring that antimicrobial drugs are being used in an appropriate manner. This participant also stated that the EU is researching the degree to which member states are taking steps against resistant pathogen strains; this further reinforced the theme of multinational actors building capacity to overcome AMR at country level.



### **The role of livestock industry partnerships**

Discussion also focused on two bodies working at the epicentre of the livestock and agriculture sectors, and the bearing that these industries have on health, development and sustainability: GASL and the LGA.

Several participants referred to the aims of each consortium and the history of their respective mandates. GASL was described as a multi-stakeholder platform intended to create a space for consensus-building around important issues including AMR. Another participant highlighted that in its earliest stages, GASL had addressed environmental issues, but stated that it now looks more broadly at issues of health, inequality and economics. GASL's activities were later said to be based on five principles: maximizing the efficiency of livestock production, while avoiding scarcities in natural resources, realizing poverty reduction, reducing the threat of disease and other associated risks, and improving governance.

It was also noted that GASL focuses on combating AMR by ensuring that the private sector, civil society and government bodies work in partnership with each other rather than in silos. This notion of collaboration was again linked to the One Health Initiative, with one participant emphasizing that integrated approaches involving stakeholders from the livestock, agriculture and human health sectors will best serve joint action targeting AMR.

The LGA was described as a consortium of organizations and actors that have a global public mandate on livestock. One participant argued that the LGA should expand to increase the participation of academia, farmers and animal welfare institutions, and that a strong link between GASL and the LGA would mutually benefit both groups' efforts to address AMR. Other participants commented that the LGA's advocacy role should be aligned with advancing the profile of livestock in the discussions to be held at the UN in 2015 as part of the ongoing process to develop a post-Millennium Development Goals, post-2015 global development framework.