RUMA® POSITION PAPER ON ANTIBIOTIC RESISTANCE AND ANTIBIOTIC USE IN LIVESTOCK

Introduction

1. There is much debate at present on antibiotic resistance in human medicine and antibiotic use in human and veterinary medicine. The Prime Minister has raised the issue and two Parliamentary Committees have considered it with various groups, including RUMA, making submissions. Most of these submissions have been balanced but a paper by the Alliance to Save Our Antibiotics (ASOA) has once again raised various assertions about the use of antibiotics in livestock that need to be addressed. This paper clarifies RUMA’s position on antibiotic resistance and how antibiotics can be responsibly used in UK livestock. It also addresses some of the inaccurate assertions in the ASOA paper.

About RUMA

2. The Responsible Use of Medicines in Agriculture Alliance (RUMA) was set up in 1997 with the aim of promoting responsible use of all medicines in agriculture. It involves organisations from across the food chain including veterinary bodies, farming organisations, the veterinary medicines industry and retailers. A list of member organisations is at Annex 1. RUMA’s work is funded entirely by members’ annual fees with an annual turnover of around £20,000.

3. One of the ways that RUMA promotes responsible use is by providing free guidelines for farmers and vets. RUMA’s responsible use guidelines stress the need for good farm management and disease prevention strategies to minimise the risk of disease and the need to use medicines and then encourage the proper treatment of animals that become ill.

4. RUMA’s guidelines are applicable to all farming production systems.

5. Antibiotic resistance is an important One Health issue and RUMA supports the initiatives on responsible use in both human and animal medicine. Antibiotics are important for maintaining the health of both humans and animals and it is vital that all parties should work together to ensure that antibiotics remain an effective tool in the treatment of humans and animals so that they continue to be available and effective when needed. The key driver for any controls on the use of antibiotics in animals is to reduce the risk of resistance in humans, be it through the provision of safe food from healthy animals and/or preventing the potential transfer of bacteria that have acquired resistance in animals to man. It is also important that we ensure that veterinary antibiotics remain effective so that animal diseases can be treated for animal health and welfare reasons.

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Antibiotic Resistance in Humans

6. Antibiotic resistance is important. There is a clinical crisis in human medicine because antibiotic resistance is making infections due to bacteria harder to treat with antibiotics. UK Chief Medical Officer Professor Dame Sally Davies said “antibiotic resistance is one of the greatest threats to modern health and we face a future without cures for infection if antibiotics are not used responsibly”.

7. Antibiotic resistance is complex. Antibiotic resistance can and does arise through naturally occurring mutations of the bacteria. Resistance factors can be transmitted to the next generation of bacteria and sometimes transfer to different species of bacteria. These resistant bacteria can spread between species including from animals to humans and vice versa and to and from the environment.

8. We know that bacteria can transfer from animals to humans and from humans to animals and that some of these bacteria could be resistant. But scientific evidence increasingly recognises that the problem of antibiotic resistance in humans comes largely from the over-use and mis-use of antibiotics in human rather than animal medicine. The Department of Health’s 5 Year Strategy on Antimicrobial Resistance said ‘Increasing scientific evidence suggests that the clinical issues with antimicrobial resistance that we face in human medicine are primarily the result of antibiotic use in people, rather than antibiotics in animals’. Fortunately, despite considerable work by Public Health England, the results of a study by the Royal College of General Practitioners found that though the proportion of cases of coughs and colds where antibiotics were used decreased from 47% in 1995 to 36% in 1999, it then increased to 51% in 2011. So there is clear and recent evidence that antibiotics continue to be mis-used in human medicine.

9. The European Centre for Disease Control also agrees that the main cause of resistance in humans is the use of antibiotics in people. Their Antimicrobial Resistance Fact Sheet for the General Public says “Certain resistant bacteria that are associated with food consumption, such as Campylobacter or Salmonella, may be transferred from animals to humans through food. People may also acquire resistant bacteria from direct contact with animals. However, the major cause of antibiotic resistance in humans remains the use of antibiotics in human medicine”.

10. The House of Commons Science and Technology Select Committee’s Report “Ensuring Access to Working Antimicrobials” says (paragraph 51) that “there is circumstantial evidence that antimicrobial resistance can be transmitted from animal pathogens to human pathogens although the evidence base is incomplete”. RUMA supports the Committee’s call for more research into this area particularly as more recent studies have found that resistant bacteria in humans and animals are genetically different which suggests that animal use of antibiotics does not contribute to human resistance. This is in direct contrast to earlier studies referenced in the ASOA report which suggests animal use is a major factor. We need to consider very carefully the consequences of reducing necessary antibiotic use in animals, which can have serious animal welfare/health implications, for possibly no benefit to reducing resistance in humans. Indeed, whilst measures in some countries such as Denmark and The Netherlands have reduced antibiotic use in animals, resistance by some bacteria in humans in those countries continues to increase and there are reports of consequent animal welfare problems.
11. However, there can be no complacency in animal use. Antibiotics must be used responsibly in agriculture to stop the possibility of their use leading to problems in animal or human medicine.

**Antibiotic Resistance in Animals**

12. Antibiotics have been a major benefit to farm animal welfare for many years. Despite the criticisms of the way antibiotics are used in animals there is no clinical crisis in animal medicine as, apart from isolated cases of swine dysentery, some penicillin-resistance in *Streptococcus suis* and some reported resistance to newer antimicrobials in respiratory pathogens of animals, antibiotics continue to work for all animal treatments. Current evidence shows that despite many years of continuous antibiotic use under veterinary supervision their use is not leading to significant resistance problems in animals.

13. Comparing the quantity of antibiotics used in humans and animals in the UK is not possible as we don’t actually know what volume of antibiotics is used in humans. However, data from the Health and Social Care Information Centre shows that 376 tonnes of just one class of antibiotic, the β-lactams, was used by GPs in England in 2012. This does not factor in other classes of antibiotic, or any of the antibiotic use in hospitals. In contrast, the total sales of all antibiotics for use in all animals, including companion animals, for the whole UK in 2012 was 409 tonnes, 82 tonnes of which were β-lactams[^11]. There is also a danger in focusing on total usage figures as this can undermine the important responsible use message that it is important to complete an antibiotic course. A simple ‘use less’ message could lead some to reduce usage by not completing the full course of treatment which increases the risk of resistance.

14. Comparison of human and animal resistance levels can be confusing and misleading as resistance is often measured differently in human and animal bacteria. In human medicine resistance is reported when the antibiotic does not work clinically, whereas in veterinary medicine resistance is often reported where there is laboratory detected reduced susceptibility, even though the antimicrobial may still be effective when used to treat a sick animal. Using the human standard of measurement would result in much lower levels of reported antibiotic resistance in animal bacteria[^12].

**Responsible Use of Antibiotics on Farm**

15. Farm animals, regardless of the management system, have a commercial value on farm, a value which is directly linked to their production capability. It is therefore in the best interest of a livestock keeper to look after his animals and to make sure that they are healthy. Much work has been done in recent years to recognise farm animals as sentient beings and to improve welfare standards. Indeed, farmers and vets have a legal obligation to meet high statutory welfare standards for the animals in their care. UK farmers have a good reputation in the EU for introducing and maintaining high welfare standards before other member states.
16. Animals, like humans, become ill and need to be treated with medicines. Also like humans, medicines are used to prevent disease and, therefore, suffering in animals. Antibiotics may only be used on farm following diagnosis and prescription by a veterinary surgeon and they are used in the following ways:

**Curative treatment (also referred to as Therapy)**

Treatment of a sick animal or group of animals following the diagnosis of infection and/or clinical disease.

**Control treatment (sometimes referred to in veterinary medicine as Metaphylaxis) – which is mostly equivalent in human medicine to Prophylaxis**

Treatment of a group of animals after the diagnosis of infection and/or clinical disease in part of the group, with the aim of preventing the spread of infectious disease to animals in close contact and at considerable risk and which may already be (sub-clinically) infected.

(A useful comparison with human medicines would be where a child in a classroom is diagnosed with meningococcal meningitis necessitating urgent treatment of all other in-contact children).

**Preventive treatment (sometimes referred to as Prophylaxis)**

Treatment of an animal or a group of animals, before clinical signs of infectious disease, in order to prevent the occurrence of disease or infection.

Preventive treatment or Prophylaxis with antibiotics:

- must only be applied to animals diagnosed at high risk of bacterial disease, and
- must only occur under prescription by a veterinarian on the basis of epidemiological and clinical knowledge, and
- must not be applied systematically or routinely, and
- must not be used to compensate for poor hygiene or for inadequate husbandry conditions or where improvements in animal husbandry could reduce the need for antibiotic treatment. Prophylactic treatment may be appropriate on a temporary basis, to prevent disease in animals while the vet and farmer make improvements to bio-security and animal husbandry on the farm, to reduce the likelihood of subsequent batches of animals requiring treatment in this manner.

17. In order to prevent residues from a medicine that could be harmful to humans a withdrawal period is set by the independent regulatory authorities who assess the medicine’s features before it can be placed on the market. This is a period of time following the last treatment during which none of the animal may be used for human consumption. After that period tests have shown that any medicinal residue in the animal will be safe for consumers.

18. RUMA supports the call from various quarters for the collection of better data on the usage of antibiotics in animals. We have basic information on total quantities of each antibiotic supplied to the market but we need more detailed information on how much antibiotic is used in each species and, ideally, why that antibiotic was used.
19. The veterinary profession has taken a strong lead in recent years in encouraging its members to adopt the responsible use of antibiotics. The British Veterinary Association (BVA) and its specialist divisions have published and promoted general guidelines and species specific guidance targeted for different sectors, some of which recommends a formulary approach to the correct selection and use of antibiotics for the many indications in the wide variety of species to be treated.

**Should Antibiotics be used to Prevent Illness?**

20. RUMA agrees with the general premise that prevention is better than cure and believes that antibiotics can be used responsibly in both human and animal medicine to prevent disease and suffering. RUMA does not, however, support the routine preventive use of antibiotics where such disease challenge can be prevented by better husbandry and farm management. RUMA published a statement on the preventive use of antibiotics in farm animals in April 2013\(^1\) and this sets out how antibiotics can be used responsibly on farm to prevent disease. Like in peri-operative human surgery there are times e.g. post weaning, when animals are more susceptible to bacterial disease which will cause suffering that can be prevented by using antibiotics.

21. The ASOA paper highlighted the benefits of the routine preventive use of antibiotics in human surgery (page 7) and yet at the same time called for a ban on the routine preventive (prophylactic) use of antibiotics in agriculture. The suggestion here is that preventive use in agriculture leads to an increased risk of resistance which could then be transferred to humans while the direct preventive use of antibiotics in humans does not! If there is scientific evidence that using antibiotics in human and/or animal medicine to prevent disease increases the risk of resistance in humans then such use of antibiotics in humans and animals should be reduced. But why do ASOA single out the animal preventive use and laud the human preventive use? This would appear to be an attack on conventional farming methods and has nothing to do with saving antibiotics, the use of which the principal movers in the ASOA, the Soil Association, spurn.

**RUMA’s Position on Agricultural Production Systems**

22. Responsible use applies to all livestock production systems used in UK farming. Farm animals have an economical function and a commercial value: fundamentally they are there to provide consumable livestock products. There is, therefore, a direct benefit to the farmer/animal keeper in providing explicit care to those animals. This care is often recognised by the emphasis on protecting and enhancing the health and welfare needs of the animal, as expressed in the Farm Animal Welfare Committee’s (FAWC) 5 Freedoms. Thus, farm animals are fed, housed, protected from predators and disease and generally provided with more beneficial resources than they would experience in their ‘natural’ or ‘wild’ state. This should be the case regardless of whether the animal is organically or conventionally managed, free ranging, outdoor or indoor housed, intensive or extensive.
23. The key defining success factor is the quality of the care and the level of knowledge and understanding of the animals’ needs provided by the animal keeper, in other words the quality of his stockmanship skills. A highly skilled stockman understands the needs of his animals and will fulfil those needs through proper management of the environment, the nutrition, breeding decisions, veterinary professional advice and the use of veterinary medicines to protect the health of the animals. RUMA therefore, has no prejudice towards any agricultural production system. All animals should be cared for in a manner that is appropriate to their breed and their surroundings. RUMA believes that the responsible use of antibiotics, and other veterinary medicines, is an important component of that care.

24. Antibiotics and other authorised medicines play an important role in preventing disease and treating sick animals. The responsible use of medicines means using medicines as little as possible and much as necessary. Farmers and their vets are working to minimise the need to use a medicine by reducing the chances of disease challenge e.g. good farm management and stockmanship, keeping animals well fed and watered, with good ventilation. Vaccination programmes and biosecurity should be part of the farm health plan. However, when an animal becomes ill it should be treated in accordance with veterinary surgeon instructions with the right medicine, at the right dose for the right length of time.

25. RUMA has concerns that the use of medicines, especially antibiotics, is being viewed as a product differential for some of the agricultural production systems, especially the organic and ‘aspirational’ production methods such as biodynamics. Veterinary medicines are an important tool in protecting the health needs of animals and the consuming public, and we do not feel that it is appropriate to politicise them in this way. Under certain regimes, antibiotics may only be used as a last resort after treatment with alternative medicines, such as herbal or homeopathic products, has failed. In other words, antibiotics with proven efficacy are preferentially withheld in favour of treatment with products of unproven efficacy. This presents a huge potential to increase or extend the animals’ suffering beyond that which is necessary or acceptable in order to appeal to the ethical wants of some consumers. There is considerable economic pressure on organic farmers not to use antibiotics as repeated doses can lead to the removal of organic status and the related financial premium. RUMA calls on the Soil Association, and others licensing organic production, to allow antibiotics, and all other authorised medicines, to be used responsibly in the interests of animal welfare.

**Should Critically Important Antibiotics (CIAs) for Human medicine be used in animals?**

26. Not all medicines considered to be critically important for human medicines are licensed for veterinary use in animals e.g. carbapenems. RUMA is unaware of any need to use such medicines in animals and would not support any change to the current situation.

27. Fluoroquinolones and 3\textsuperscript{rd} and 4\textsuperscript{th} generation cephalosporins are authorised for livestock use and form an important part of the veterinary surgeon’s armoury in treating animal disease. Removing any antibiotic from animal use will put more pressure on the antibiotic classes used in its place thus increasing the likelihood of resistance developing. However, the CIAs should be used sparingly and not routinely as first choice antibiotics in animals as set out in RUMA’s preventive use statement i.e.
- They should be used to treat animals but not be used as 1st line treatment and then only after susceptibility testing of the diseased animals or previous experience and laboratory history of that farm has shown other classes of antibiotic to be ineffective.
- They should almost never be used to control a disease outbreak in a group of animals, the only exception being cases when no alternative is available or feeding systems mean healthy animals have to be treated along with sick animals which, ideally, should be isolated/treated separately if possible.
- They should not be used preventively apart from dry cow therapy which is not known to lead to resistance issues.

28. The dry cow period is a risk period for intramammary infections and vets and farmers should have strategies to prevent and/or treat infections for this period. Mastitis is a bacterial infection that can affect all mammals. It can be extremely painful in humans and dry cow therapy can be vital to avoid suffering in dairy cows. A responsible strategy for the dry cow period is to include a review of the epidemiological history of herd health as a whole, and each animal individually, following diagnosis by a vet based on the animal's Somatic Cell Count, and her mastitis history. Treatment can include teat sealants to prevent bacteria entering the udder and/or antibiotic tubes to suppress the infecting bacteria. There is no evidence that antibiotic use in dry cow tubes leads to resistance. Some antibiotic tubes include 3rd generation cephalosporin as the active ingredient and there is no evidence to show that their use as an intramammary preparation has resulted in a change in antimicrobial resistance patterns. Vets and farmers should regularly review all products, including 3rd generation cephalosporins, and amend their strategy accordingly.

29. Cephalosporins, primarily the third and fourth generation ones, are not regularly used in pig medicine in the UK, unlike in many EU countries, which have used them routinely after surgical castration of piglets during the first week of life. In the UK it is estimated that only 1-2% of piglets are castrated. The cephalosporins are exceptionally effective products and are occasionally used for the treatment of acute pleuropneumonia, 'greasy pig' disease and infectious arthritis, when indicated by antimicrobial sensitivity testing and when all other medications have failed.

30. With so few authorised medicines available for vets to treat the wide range of diseases that can affect the large number of animal species, the prescribing cascade is a vital decision tree to help vets prescribe the right medicine when no authorised product is available to treat the specific disease in the affected species. Vets follow the principles of the cascade when prescribing the off-label use of medicines however, RUMA recognises the difficulty of determining the correct dose when using cephalosporins off-label and recommends that their off label use is avoided.

31. Fluoroquinolones are rarely used in poultry in the UK. Commercial poultry producers and veterinarians acknowledge the importance of these products for human medicine. Therefore, only in the exceptional circumstances where other therapeutic options have failed, animal welfare is compromised and on the basis of antimicrobial sensitivity testing will treatment with fluoroquinolones be considered. The ASOA proposed ban on fluoroquinolone use in poultry would remove this limited use opportunity from vets jeopardising animal welfare.
Independence of Regulatory System

32. Human and animal medicines are regulated in the same way. Veterinary pharmaceutical companies have to carry out tests to international standards to show their medicine is safe (to the animal, people handling the animal or eating its produce and the environment), works effectively and can be manufactured repeatedly to the same standards. The only difference from human medicines is that they do not have to show safety for consumers!

33. To ensure independent scrutiny of the data provided by the human and veterinary pharmaceutical companies the Government requires expert Civil Servants to assess them. The Government requires the companies to pay fees to cover the cost of this work. In their report the ASOA has implied that because the companies pay for the assessment work they have undue influence over the regulators. RUMA is not aware of any foundation for this slur on the integrity of the staff of the Veterinary Medicines Directorate (VMD) and by implication their human medicine equivalent. The VMD is part of the UK Civil Service which is widely recognised for its high integrity and professionalism and the VMD is considered a world leader in veterinary medicines regulation. The VMD has issued an objectivity and impartiality statement and all VMD staff work to the Civil Service Code which requires adherence to the principles of honesty, independence and integrity.

RUMA

September 2014
References

1. Antimicrobial Resistance – why irresponsible use of antibiotics in agriculture must stop – a briefing from the Alliance to Save Our Antibiotics


8. M de Been et al. ECMID 2013 Whole genome sequence-based epidemiological analysis of ESBL-producing Escherichia Coli’

9. DANMAP 2012 Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark. ISSN 1600-2032


12. The European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2011 (EFSA Journal 2013; 11(5):3196 [359 pp]). This report found that for some bacteria “little or no resistance is reported using the CLSI clinical breakpoint in any isolates from food or animals, whereas the situation is often quite different when the EUCAST epidemiological cut-off value is applied to the same isolates to determine resistance”.

14. The prescribing cascade is a provision in the Veterinary Medicines Directive 2001/82 that recognises the lack of authorised medicines available to treat all diseases in all species. It allows vets, exceptionally, to use a medicine authorised for a different disease and/or species, imported from another Member State, authorised for human use, or to be made up to treat an animal to protect animal welfare.

15. VMD Statement of Objectivity and Impartiality

ANNEX 1 List of RUMA® members September 2014

RUMA membership is open to all organisations with an interest in the areas of food safety, animal health and animal welfare. Current RUMA members are:

Agricultural Industries Confederation (AIC)
Animal Health Distributors Association (AHDA)
Animal Medicines Training Regulatory Authority (AMTRA)
Assured Food Standards (AFS) better known as Red Tractor Assurance
British Egg Industry Council (BEIC)
BPEX and EBLEX
British Poultry Council (BPC)
British Retail Consortium (BRC)
British Veterinary Association (BVA)
City and Guilds Land Based Services
DairyCo
Dairy UK
Game Farmers’ Association (GFA)
Linking Environment And Farming (LEAF)
National Beef Association (NBA)
National Farmers’ Union (NFU)
National Office of Animal Health (NOAH)
National Pig Association (NPA)
National Sheep Association (NSA)
NFU Scotland (NFUS)
Royal Association of British Dairy Farmers (RABDF)
Royal Pharmaceutical Society (RPS)
Royal Society for the Prevention of Cruelty to Animals (RSPCA)

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