

ANTIBIOTICS AND ANTIBIOTIC RESISTANCE IN VETERINARY SCIENCE

A guide to understanding the issue
and avoiding inaccurate or misleading
information



Introduction

Long before antibiotics were used in medicine, there were antibiotic-resistant bacteria. Organisms have evolved natural defence mechanisms – such as antibiotic substances – to modify their bacterial environment. In reaction, these bacteria developed mechanisms to contend with these antibiotic substances. Strains of bacteria with the ability to inactivate modern antibiotics have been discovered in silt deposits dating back 30,000 years. So the phenomenon of multidrug-resistant bacteria, which is creating such concern for public health officials across the world, is neither new, nor is its origin necessarily a product of human activity. It does remain, however, a serious threat to global public and animal health, requiring concerted action from policymakers, scientists, industry, vets, farmers, medical doctors, as well as the general public.

What is certainly true is that the use of antibiotics in human and veterinary medicine creates the

conditions that allow resistant strains of bacteria to prosper. In any community of bacteria – usually millions of individual organisms - there will be some that have undergone genetic mutations which improve their ability to survive treatment with particular antibiotics. If exposed to those antibiotics, these bacteria will grow in numbers to take up the space and resources that are left as more susceptible strains are killed off. Changes in the composition of the bacterial population are inevitable without careful management of the medicines used against them. They will occur more quickly if patients are given the wrong antibiotic or the wrong dose or don't complete their course of treatment.

With the growing awareness of the potential impact of antibiotic resistance on human health through the emergence of difficult to treat infections, urgent efforts are being made to tackle the problem. Ensuring more judicious use of antibiotics is

one key element to any strategy for controlling resistance, as it will reduce the evolutionary pressures that lead to the emergence of these potentially hazardous bacterial strains.

Although the scientific evidence points to the use of antibiotics in human medicine as by far the most important factor promoting resistant strains in human medicine, their application in livestock production has also attracted attention. Certain campaign groups have been responsible for promoting a number of misconceptions about giving antibiotics to animals. Some groups back their arguments with questionable scientific claims.

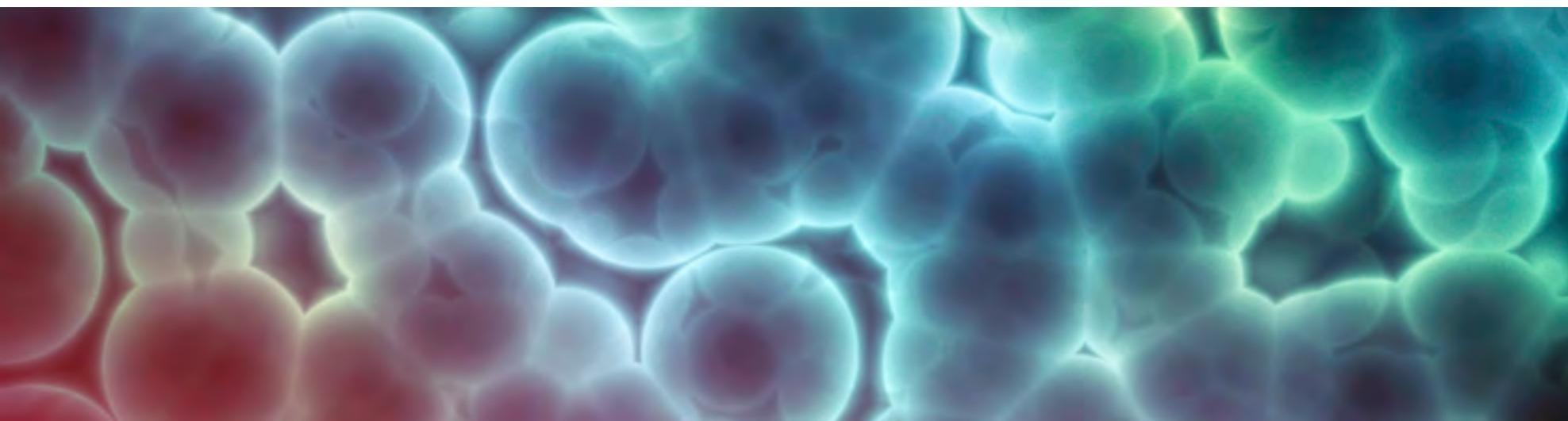
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Among the many misconceptions about the role of antibiotics in agriculture are the allegations that:

1

Antibiotics are only given to boost growth



NOT TRUE Antibiotics are used in farm animals for exactly the same reasons that they are used in humans – to prevent and treat diseases. All so-called growth-promoting antibiotic products were banned throughout Europe in 2006, and uses of medically important antibiotics to improve weight gain and feed efficiency will be withdrawn in the US and Canada over the next two years. Other major agricultural economies have adopted similar policies. Antibiotics were sometimes used at lower concentrations in feed given to cattle, pigs and poultry to control the bacteria in the gut which caused low level diseases which prevented the animals from developing at their optimum rate. This was apparent when Denmark became the first country to introduce a ban on these products. Danish farmers suffered much greater losses to death and disease in young piglets and initially had to double their use of antibiotics to treat them.¹

2

Antibiotics are only used to cover up poor husbandry



NOT TRUE Many consumers express concerns that in modern agricultural units, pigs and poultry are kept indoors at higher densities than in traditional systems. The inference is that closely packed and stressed animals will succumb to more disease and need more antibiotics. However modern agricultural units flourish because the animals are productive. They are only productive if they are healthy and not stressed.

In general poor welfare can be a primary predisposition to diseases and may affect health by altering the animal's susceptibility to disease. Changes in the livestock industry have had positive consequences like greater hygiene and bio-security that reduce the risk of disease infection. Keeping pigs and poultry indoors allows farmers to maintain conditions that will protect the health and welfare of their animals – for example, keeping out predators, such as foxes, wild rodents and birds that can introduce infectious diseases. But whichever farming system is used, once a new disease is introduced into a social group it will spread rapidly because animals have contact with each other and use the same water and food troughs. Responsible use of antibiotics helps to control any bacterial disease that does appear, and can be particularly valuable in protecting healthy animals during weaning or transportation, when their normal immune defences may be lower.

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Farm animals are a major source of human-resistant infections



Resistance is easily transmitted from animals to humans



Critically important antibiotics are used routinely in livestock



Antibiotic residues are often found in food

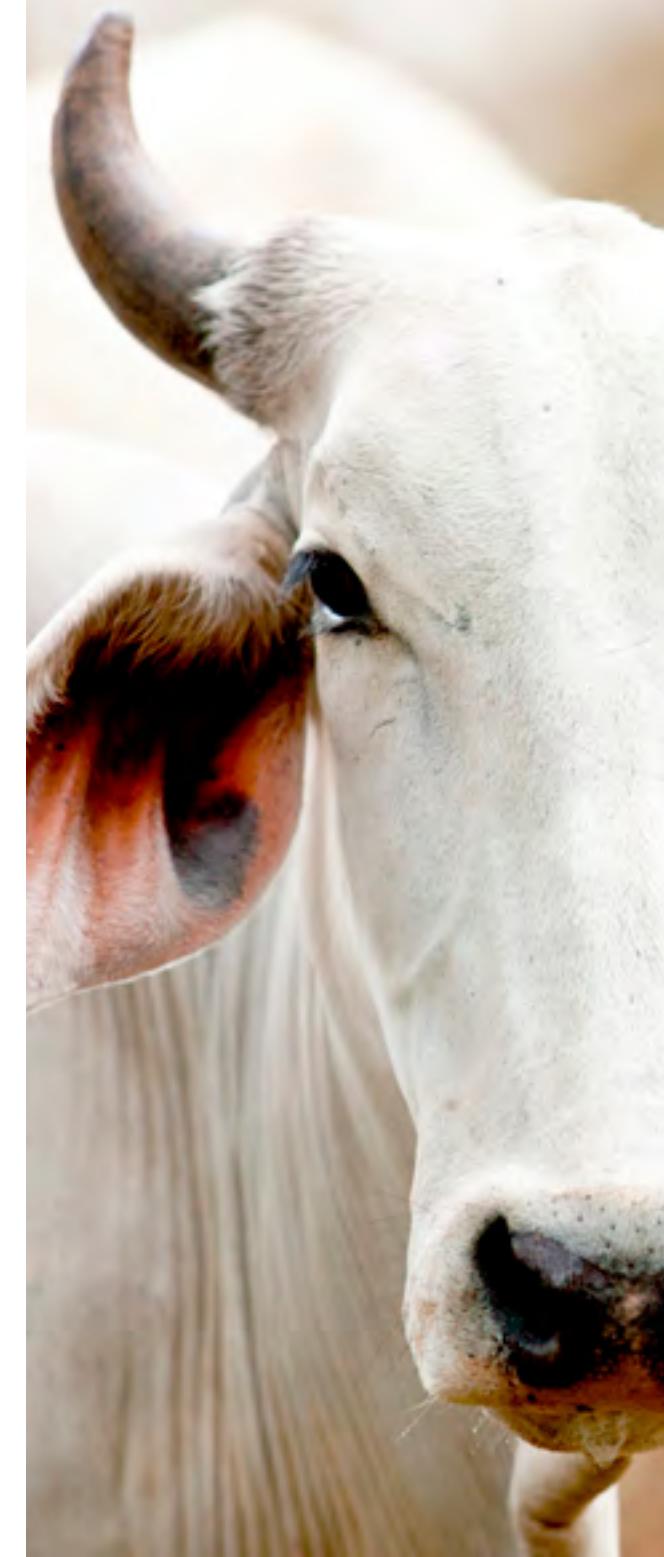


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Farm animals are a major source of human-resistant infections



NOT TRUE Some strains of antibiotic-resistant bacteria are found in farm animals and there is a theoretical risk that they could cause health problems in people, either by direct transmission from animal to human, bacterial contamination of food or by resistant genes exchanged between animal and human bacterial strains.

Although farmers and veterinarians acknowledge that these risks do exist, it is clear that they are not an important factor in the development of multi-drug resistant bacterial infections in people. Overwhelmingly, the scientific evidence shows that hospital patients with these kind of infections contracted the disease from other people or from contaminated surfaces in the hospital environment. Indeed, a US Centers for Disease Control (CDC)² report in 2013 listed 18 strains of antibiotic-resistant bacteria which pose a threat to human health. Only a few of these are a potential animal source for resistant strains, like *Salmonella* and *Campylobacter*. These bugs are omnipresent in the environment and can cause unpleasant gastrointestinal infections whether the strain is resistant or not. Any risk can be effectively eliminated by good kitchen hygiene and proper cooking of all meat and dairy products.³

4

Resistance is easily transmitted from animals to humans



NOT ACCURATE The majority of bacteria are adapted to living on a particular host species and so a strain of bacteria found in cattle or sheep is unlikely to survive in humans. So there was some surprise when a series of studies in different countries found bacteria resistant to the same range of antibiotics in people and animals⁴. However, more recent studies using more precise analytical techniques in Scotland and the Netherlands have found that the genes causing resistance in the different species are actually quite distinct, meaning the resistant strains must have emerged independently.⁵



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Critically important antibiotics⁶ are used routinely in livestock



NOT ACCURATE

One major class of veterinary antibiotics is the tetracycline group which makes up 40% of the total market. These were one of the first antibiotics to be developed and in many countries have limited use in human patients only. But despite their use in animals, veterinarians have found little evidence of resistant strains causing hard to treat infections in their animal patients.⁷ There is overlap in the use of medically-valuable antibiotic groups such as macrolides, fluoroquinolones and cephalosporins; the latter is only used for individual animal treatment. Veterinary fluoroquinolones, for example, make up less than 1% of all antibiotic use in US agriculture. In Europe this is just over 2%.⁸ These are effective treatments for cattle and pigs with respiratory diseases but are only available for use through a veterinarian's prescription. When used appropriately, the likelihood of fluoroquinolone-use in cattle giving rise to an untreatable bacterial disease in a human patient is vanishingly small – one recent study calculated that they would occur at a rate of a single case of Salmonella every 293 years in the US.⁹

6

Antibiotic residues are often found in food



NOT ACCURATE

Monitoring the safety of the national food supply is a fundamental responsibility for all governments. Tests are carried out on routine samples looking for residues of various types of antibiotics as well as other potential contaminants, like pesticides or toxic heavy metals. National survey results in the US and Europe typically find a rate of positive samples in all these tests of substantially less than 1%.¹⁰ This is because any authorised medicine used in livestock will have a statutory withdrawal period stating the minimum amount of time that must be observed after treatment before meat, milk or eggs from that animal can enter the food chain. If contamination does occur, it is usually due to a mistake or oversight and not deliberate, as the penalties can be quite high.



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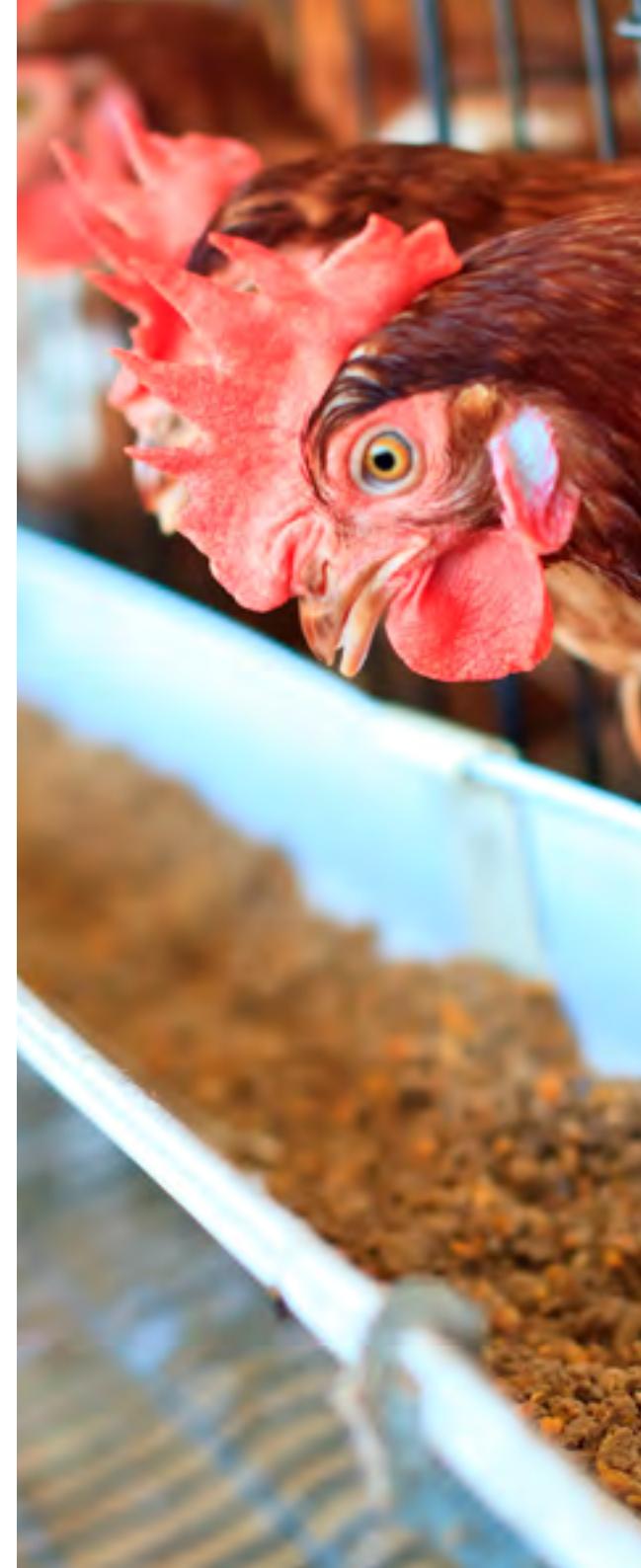
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Organic producers don't use antibiotics



NOT ACCURATE Overall antibiotic use is lower on organic units but in some countries antibiotics can be used to treat bacterial infections in both organic and conventional farming systems. Failure to deal with a condition likely to cause sickness and death in an animal is morally unacceptable, makes no commercial sense and in some countries is illegal. Under the marketing regulations operating in some countries, products from an animal that has received veterinary medicines can no longer be labelled as organic and would enter the same distribution network as products from conventional livestock production methods. In the US certified organic producers are prohibited from using any antibiotics but frequently they operate a dual system whereby the animals that need (antibiotic) treatment can be moved from organic to conventional production.



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Inaccurate claims, such as the above, made by politically-motivated campaigners or researchers are sometimes magnified by news organisations and processed into “attractive” headlines. Most people don’t have the scientific training to distinguish between accuracy and falsehood in a scientific paper but there are some pointers that will help in uncovering the truth. They include:

Inaccurate and sloppy estimates



There is no escaping the fact that most scientific papers are pretty dull for anyone who is not an expert. So those given the task of writing press releases about a research study will often liven things up to garner media attention.

Example:

An article in the Daily Mail, a UK tabloid newspaper, based on a Soil Association press release, claimed that 1,500 people in Europe and 280 Britons would be killed that year by *E coli* bacteria bearing the ESBL (extended spectrum beta lactamase) gene. This estimate was wrong. It did not account for differences between the classes of antibiotics used in the various countries, but more importantly it was based on a flawed genetic analysis. They had already withdrawn their earlier claim of finding the same genes for cephalosporin resistance in humans, poultry and chicken meat. Further analysis has shown significant genetic differences between the human and animal strains, indicating that any transfer of resistance of birds and humans would be a “rare event.”

Inappropriate methods



Claims that outwardly respectable organisations are involved in deceit should undergo a thorough and professional examination before being made public.

Example:

The Baltimore Sun newspaper ignored this advice when it told its readers that antibiotic products banned for use in poultry in 2005 were still being used by US chicken farmers seven years later.¹¹ The allegation was based on a study by researchers at Johns Hopkins University which analysed samples of feather meal, a by-product of the poultry meat industry used mainly as fertiliser. The rendered down feathers of slaughtered chickens were found to contain residues of various fluoroquinolone antibiotics, suggesting that farmers were defying the ban. Yet due to the remarkable sensitivity of modern analytical methods, the product was also found to contain residues of caffeine, antihistamines and the antidepressant Prozac. Since none of those products are supplied to broiler chickens, the likely explanation was that they came from human sources, through contamination of the ground water used in processing the feathers.¹²



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Leading or vague assumptions



It doesn't always need a deliberate falsehood to mislead. Sometimes it's only necessary for two facts to be mentioned in adjoining sentences for casual readers to assume that there is a link between the two.

Example:

One of the issues regularly highlighted by the organic farming movement is the amount of antibiotics used in farming, often said to be 70% by weight of the total market. Unless told otherwise, readers will usually make an assumption that farming contributes a similar percentage to the overall risks from resistant bacteria. But as pointed out already, the products used in human and veterinary treatments are often not exactly the same. Many of the products used in livestock were introduced decades ago, are generally less potent than modern medicines and so have to be used in higher doses. A further reason why comparisons of the tonnage of antibiotics used in the human and animal health markets are meaningless is that a fully grown beef bull could weigh the same as up to six average adult humans, so it will need a larger dose. Taking all these factors into account, a paper published in the American Veterinary Medical Association Journal¹³ estimates that an equivalent dose of antibiotics used in animals is only a tenth of that in humans.

Confusion of cause and correlation



Finding resistance to the same antibiotics in bacteria found in livestock and people provokes a knee-jerk response from advocates of organic farming, calling for bans on using antibiotics in animals.

Example:

There was an outcry following the publication of a study by a group at Denmark's National Food Institute¹⁴ pointing out correlations between resistance to *E coli* bacteria in human, cattle and poultry in 11 European countries, in a specific class of antibiotics. As a published response letter pointed out¹⁵, the researchers had committed a basic scientific error by jumping to the conclusion that animal to human transfer was the only possible explanation for these findings. The letter stated that there are background levels of antibiotic resistance everywhere in the environment, due to both human and animal usage and that transfer of the relevant resistance genes could go either way. In this Danish study, they pointed out that it is far more likely that resistance to the antibiotics originated in the human population which used antibiotics and was then passed on to animals (where this class of antibiotics was not used).



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Extrapolating from a too narrow data set

The assumption that the lessons from a study of one group can be applied to another, entirely separate population is a common mistake, and an indication of overextension.

Example:

A paper published in spring 2015 in a prestigious US journal, *Proceedings of the National Academy of Science* (PNAS) entitled “*Global trends in antimicrobial use in food animals*”¹⁶ attempted to estimate the growth in use of veterinary antibiotics in 228 countries based on the figures available from 32 countries. There was not enough data, and the available data comes overwhelmingly from high income countries. Nonetheless the article drew widespread conclusions about low/middle income countries. One critic of the paper commented: “*Extrapolation based on little and inappropriate data is speculation and misleading.*”



Unreplicated results

Most papers published in learned journals go through a peer review process that might be expected to filter out studies based on unsatisfactory scientific methods or analysis. Unfortunately they sometimes don’t.



Example:

The paper in PNAS in the previous example committed the further sin of cherry-picking the results of a paper to suit the authors’ agenda. The paper made the dubious claim that food produced by intensive farming methods was of inferior nutritional quality compared with organic produce. This was based on the conclusions of a single published study. Meanwhile, a meta-analysis¹⁷ comparing the findings from 240 studies looking at the nutritional content of meat, fruit and vegetables produced by organic methods reached entirely different conclusions. It found that there were no significant advantages in consuming organic produce compared with a conventional diet.



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Invented statistics

Studies published in respectable journals will go through the tedious but necessary process of gathering and evaluating evidence. Sometimes statistics are wrongly used or not even used at all. An alternative approach is to simply make up the statistics needed to support one’s argument.

Example:

The website *Underground Health Reporter*¹⁸ refused to let the facts get in the way of a good story with the invented claim that half of all supermarket meat tested in the US was contaminated with antibiotic-resistant bacteria. It recommended that consumers should therefore choose the more expensive but otherwise almost identical organic option. This was rebutted by the FDA which stated that the underlying report, “oversimplifies”... and... “provides misleading conclusions.”¹⁹



Suggested secret influence

If there is any doubt about the availability of the scientific evidence needed to back up a particular claim, then there is always the option – widely used in political circles – of attempting to undermine an opponent’s credibility. This is a low-cost strategy.



Example:

The UK-based campaign group ASOA (Alliance to Save Our Antibiotics) claimed that antibiotic manufacturers are able to exert undue influence over the national medicines regulatory body – the UK Veterinary Medicine Directorate – as that agency charges companies for the process of examining data on the safety, quality and efficacy of their products. This claim is unworthy of analysis since it is common around the world for the animal health industry to bear some of the costs of regulatory oversight. It is an unwarranted slur on an internationally respected government organisation, as well as on manufacturers.²⁰



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Antibiotics not only cure bacterial diseases in people, they also cure bacterial diseases in animals. In doing so, they help fulfil our moral obligation to the animals in our care. Antibiotics have a role to play in sustainable livestock production by preventing waste and inefficiencies caused by disease, and help provide a safe supply of food from healthy animals. They keep our pets healthy thereby allowing a continued strong human-animal partnership.

Antibiotics should always be used responsibly, under veterinary prescription, and only when necessary. They are powerful tools and their benefits need to be preserved for future generations. Consequently, they should always be handled in such a way that limits their potential for stimulating the development of resistant bacterial strains.

This requires correct policies and strategies. Informed decision-making is dependent on reliable facts and must be able to distinguish these from

myths and tactics which misinform and mislead policy-makers and the public.

By themselves, antibiotics are not a panacea for dealing with health problems in man or animal, but there will always be a need for them. In the future new veterinary antibiotics will need to be made available under the right conditions as explained in this section. Veterinarians, farmers and pet owners must appreciate that effective disease control does not rely on one class of medicines alone. It requires a balanced approach involving careful attention to good hygiene, nutrition and the use of other preventive measures such as vaccination.

We have always lived with bacteria and always will. We need to study them and see how we can control their dissemination, while at the same time manage our use of antibiotics, vaccines and all veterinary medicines in order to maintain their efficacy.

HealthforAnimals is a non-profit, non-governmental organisation representing manufacturers of veterinary pharmaceuticals, vaccines and other animal health products throughout the world, as well as the associations that represent companies at national and regional levels (referred to as Members).

The animal health industry provides value to society by protecting animals and as a consequence, humans, from disease. Our products help keep pets and farm animals healthy. The public health benefits we bring include safer and more secure food supplies, more efficient production for increased food security, improved sustainability, and prevention of the transmission of zoonotic diseases.

For further information on HealthforAnimals, please visit www.healthforanimals.org and follow us on Twitter @Health4Animals

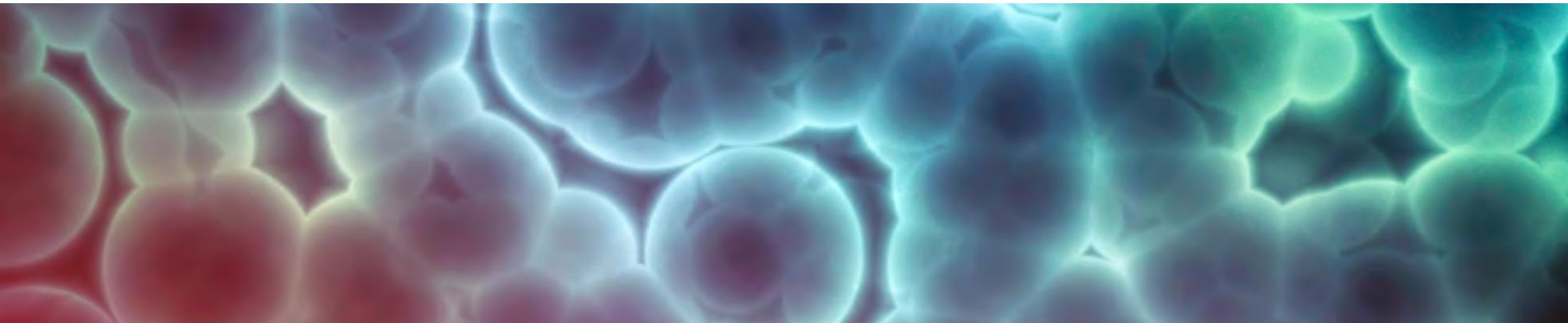
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168 Avenue de Tervueren, Box 8
1150 Brussels, Belgium

info@healthforanimals.org

 @Health4Animals

www.healthforanimals.org