Developing Antibiotic Stewardship in Animal Agriculture

Executive Summary

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The miracle drug of the 20th century is in danger of running out of power. In June 2012, at the G8 Summit in London, scientific ministers from the world's eight most powerful countries issued a statement calling antimicrobial resistance (AMR) "a major health security challenge of the twenty first century." [1] AMR is resulting in increased human mortality and increased hospital stay lengths globally. The evolution of resistance is a natural phenomenon that happens when microorganisms are exposed to antimicrobial drugs, and resistant traits are exchanged between certain types of bacteria. While the complete epidemiological picture is highly complex, involving antimicrobial use in humans, animals and the environment, the World Health Organization (WHO) states "the misuse of antimicrobial medicines accelerates this natural phenomenon." Furthermore, new resistance mechanisms are "making the latest generation of antibiotics virtually ineffective." [2]

Antimicrobial use is an integral part of many industrialised livestock production systems. The sometimes indiscriminate use of antimicrobials in animal agriculture has come under scrutiny from governments, companies and consumers who are concerned with preserving the ever-diminishing arsenal of antimicrobials that work in humans, for as long as possible. The difficulties associated with quantifying the contribution of animal agriculture to the overall problem of AMR in human health inevitably complicate policy making, and have fuelled debate over the use of antibiotics on farms. However, in order to slow down the dangerous development of resistance, Benchmark Sustainability Science urges all relevant actors to use antibiotics more responsibly — both in humans and in livestock.

1. www.gov.uk/government/news/g8-science-ministers-statement
2. www.who.int/mediacentre/factsheets/fs194/en/

Critically Important Antibiotics

This report provides an overview of current practice — and quantity of use — of antibiotics the WHO has determined to be Critically Important (CI) to humans in the UK and US. Currently there are products licensed for use in food producing animals in three of the four groups featured on the WHO's current "top priority" CI list:

- Quinolones
- 3rd and 4th generation Cephalosporins
- Macrolides

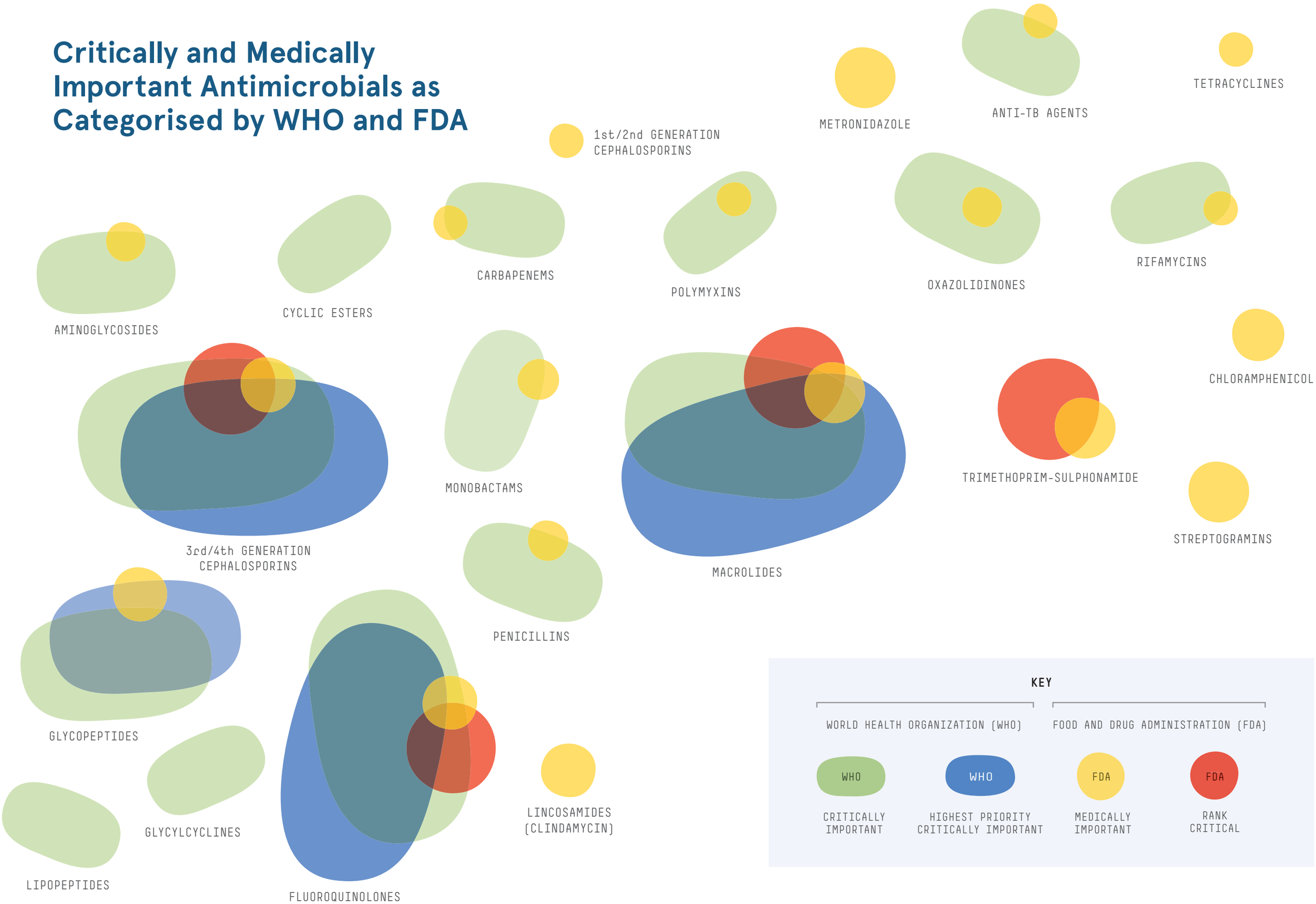
In Europe, avoparcin, (a glycopeptide — the fourth group on the WHO's current "top priority" CI list) was widely used as a growth promoter until it was banned in 1997. It was never licensed for use in the US. Other antibiotics are however, still widely used as growth promoters in the US in contrast to the EU, where all antimicrobial growth promoters have been banned since 2006.

In the US, the Food and Drug Administration (FDA) issued new voluntary Guidance for Industry (GFI #213) in December 2013, aimed at phasing out the use of what they consider "medically important" antimicrobials for growth enhancement. The key tools identified are to increase veterinary oversight and request that pharmaceutical companies voluntarily modify the approved conditions of use. In the UK, the Department of Health has recently published a UK Five Year Antimicrobial Resistance Strategy, which sets out a cross-government strategy, and a list of actions that include animal agriculture, aimed at slowing down the development and spread of AMR.

Current Use

When, in an attempt to quantify the extent of the current use of antibiotics in the UK and the US, it was found that data availability is limited, particularly in the US. Sales of the critically important antibiotics are addressed in this report, but species-specific data is currently unavailable in both countries. Data suggests that, in the UK, the greatest overall use of all types of antibiotics is in the pig and poultry sectors. In the US there are CIs (macrolide products) available for use in feed and/or water for pigs, poultry and cattle, and current licence indications include growth promotion. This results in potentially large-scale usage in these sectors. However, US antimicrobial usage data currently available to the public is inadequate, making it difficult to garner any meaningful analysis of existing use — by species or by antimicrobial class — or to measure any impact the new FDA Guidance for Industry will have. In human medicine the use of the Defined Daily Dose (DDD) unit has become universally accepted. Benchmark Sustainability Science supports the recent recommendation from the European Medicines Agency (EMA) to assign daily dose and treatment course dose values for pigs, poultry and cattle as a first step towards establishing a similar system for animal health.

Critically and Medically Important Antimicrobials as Categorised by WHO and FDA



KEY

WORLD HEALTH ORGANIZATION (WHO) | FOOD AND DRUG ADMINISTRATION (FDA)

WHO	WHO	FDA	FDA
CRITICALLY IMPORTANT	HIGHEST PRIORITY CRITICALLY IMPORTANT	MEDICALLY IMPORTANT	RANK CRITICAL

Antimicrobial Stewardship

The goal of this report is to expand the framework of antimicrobial stewardship in animal agriculture. Benchmark Sustainability Science believes that this is crucial in order to preserve the efficacy of antimicrobial agents that are currently available to humans, while at the same time ensuring our animals are healthy and our food is safe. Antimicrobial stewardship rests on three pillars:

1.

Prevention

Minimising pathogen exposure through management and hygiene measures, and optimising animals' resistance to disease.

2.

Optimising drug administration practices

Developing new and rapid diagnostics, and encouraging veterinary involvement in drug selection, dosage and duration.

3.

Collecting data

Industry and national authorities have a joint responsibility for a) collecting usage data in order to facilitate analysis, and b) the monitoring of different types of antimicrobial use at farm, species, sector, national and international level.

Unless, in the next few years, there is clear evidence that the livestock industries are substantially changing their practice, it is likely that governments — in response to public concern — will introduce regulative restrictions on antimicrobial use. It is also probable that if reductions in antimicrobial use were to be enforced without other changes to standard farming practice being introduced, there could be severe consequences for industry, animals and consumers, including increased disease and reduced productivity. Benchmark Sustainability Science works with livestock producers, retailers and pharmaceutical companies to help further develop the concept of antimicrobial stewardship, and to help those industries take immediate action to achieve more responsible antimicrobial use at farm level.

Antimicrobial Use by Livestock Sector in UK and US

Administration Key

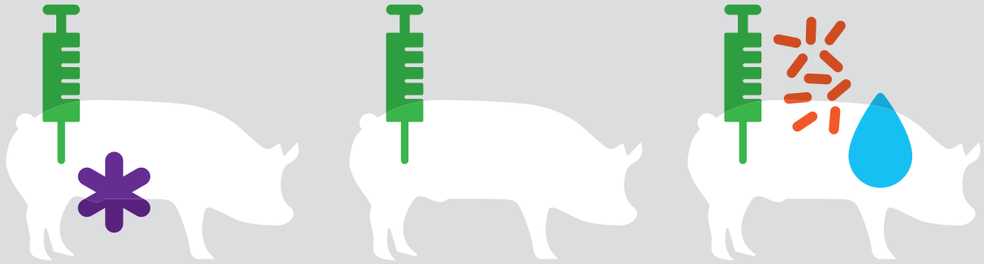
In Feed

Injection

In Water

Other

Pig UK



Fluoroquinolones
- Piglet Oral Doser

3rd/4th Generation Cephalosphorins

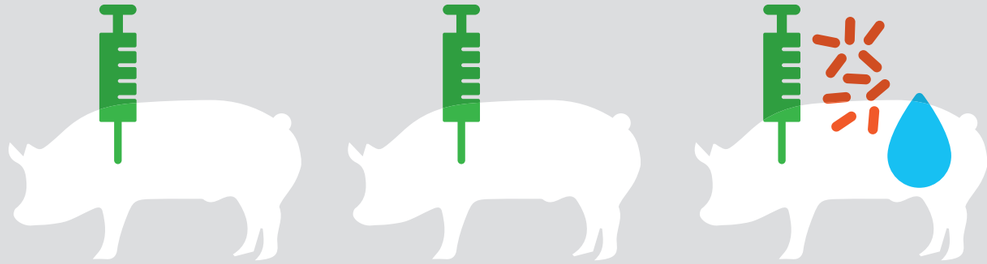
Macrolides

In December 2012, there were approximately half a million breeding pigs in the UK, but in comparison, nearly 4 million fattening pigs ***(Defra 2013a)***.

In pig production, respiratory and enteric diseases of growing pigs are likely to represent the commonest indications for antimicrobial use, which are most likely to be administered in the feed, or possibly in water.

Summary of the availability of licensed fluoroquinolone, 3rd/4th generation cephalosporin and macrolide products and their routes of administration for use in pigs in the UK. **Source NOAH 2013, VMD 2013a.**

Pig US



Fluoroquinolones
- Over the counter products are available

3rd/4th Generation Cephalosphorins
- Over the counter products are available

Macrolides
- Over the counter products are available
- Products requiring Veterinary oversight are available

In 2012, in excess of 10 million tonnes carcase weight of pork were produced in the USA ***(USDA 2013)***.

In pig production, growth promotion and improvements in feed conversion efficiency, together with respiratory and enteric diseases are likely to be the commonest reasons for antimicrobial use, which are most likely to be administered in feed or in water.

Summary of the availability of licensed fluoroquinolone, 3rd/4th generation cephalosporins and macrolide products and their routes of administration for use in pigs in the USA.**Source FDA 2014.**

Poultry UK

Fluoroquinolones

3rd/4th Generation Cephalosphorins

Macrolides

In 2012, 873 million broiler chickens were slaughtered in the UK ***(Department for Environment, Food and Rural Affairs).***

In broiler production, treatment of enteric/septicaemic infections associated with E. coli, necrotic enteritis (C. perfringens), dysbacteriosis, coccidiosis and acute and chronic respiratory infections are likely to represent the commonest reasons for antimicrobial prescriptions.

Summary of the availability of licensed fluoroquinolone, 3rd/4th generation cephalosporin and macrolide products and their routes of administration for use in chickens in the UK. **Source NOAH 2013, VMD 2013A.**

Poultry US

Fluoroquinolones

3rd/4th Generation Cephalosphorins

- Products requiring Veterinary oversight are available

Macrolides

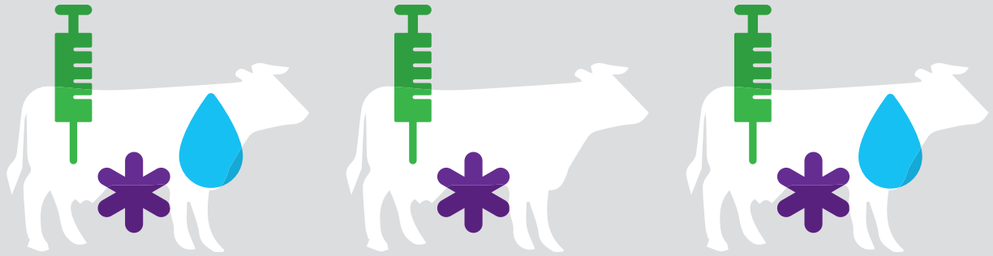
- Over the counter products are available

In 2012, in excess of 16 million tonnes of broiler meat and in excess of 2.5 million tonnes of turkey meat were produced in the USA ***(USDA 2013).*** In the month of August 2013 alone, US egg production was just under 7 billion eggs ***(American Egg Board 2013).***

In the meat production sector (broilers and turkey), antibiotics are likely to be administered for growth promotion, and disease control, including respiratory disease, coliform infections, and necrotic enteritis. In laying hens, a limited number of antibiotics are licensed for disease control and to increase egg production and feed conversion efficiency.

Summary of the availability of licensed fluoroquinolone, 3rd/4th generation cephalospins and macrolide products and their routes of administration for use in poultry in the USA. **Source FDA 2014.**

Dairy and Beef UK



Fluoroquinolones
- Calf Bolus

3rd/4th Generation Cephalosphorins
- Intra-Mammary Inc. Dry Cow Therapy

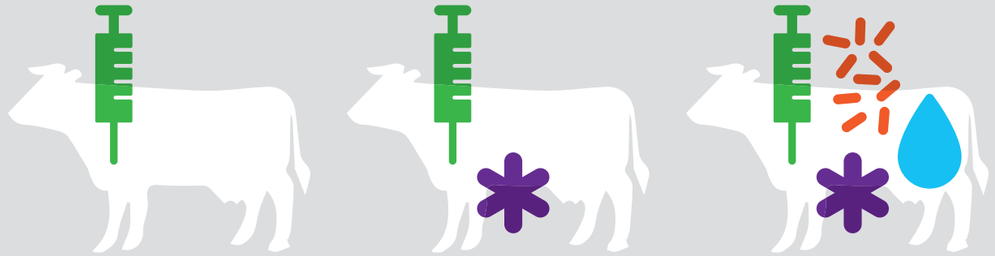
Macrolides
- Intra-Mammary

In December 2012, the size of the UK dairy herd was 1.8 million and the beef herd 1.6 million ***(DEFRA 2013A)***.

Mastitis, lameness, post-calving uterine infections and calf pneumonia/diarrhoea are the commonest indications for antimicrobial prescriptions.

Summary of the availability of licensed fluoroquinolone, 3rd/4th generation cephalosporin and macrolide products and their routes of administration for use in cattle in the UK. **Source NOAH 2013, VMD 2013A.**

Dairy and Beef US



Fluoroquinolones
- Products requiring Veterinary oversight are available

3rd/4th Generation Cephalosphorins
- Intra-Mammary for Lactating and dry cows
- Products requiring Veterinary oversight are available

Macrolides
- Subcutaneous Implant with Trenbolone and Oestrdiol
- Over the counter products are available

In 2012, just under 12 million tonnes carcase weight of beef and veal were produced in the USA. ***(USDA ERS 2012)***.

The major indications for antimicrobial administration in beef cattle, specifically feedlot cattle, include growth promotion, increasing feed conversion efficiency, controlling liver abscesses, bovine respiratory disease (BRD or shipping fever) and lameness.

In the dairy sector, major reasons for antimicrobial administration include mastitis, lameness and post-calving uterine infections. In both sectors, neonatal calf diarrhoea may also be a common indication for antimicrobial therapy.

Summary of the availability of licensed fluoroquinolone, 3rd/4th generation cephalosporins and macrolide products and their routes of administration for use in cattle in the USA. **Source FDA 2014.**

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