



## INFORMATION NOTE ON ANTIBIOTIC RESISTANCE AND THE RESPONSIBLE USE OF ANTIBIOTICS IN FARM ANIMALS

*This note has been produced by RUMA to provide an introduction to the issue of antibiotic resistance and the principles of responsible use of antibiotics in animals.*

### Content

1. Explain antibiotic resistance and why it matters to human and animal health
2. Set out why and how antibiotics are used in UK farms
3. Identify the risks to public health from use of antibiotics in farming
4. Explain the responsible use of antibiotics in farming

### The scope of Antibiotic Resistance in this note

Despite generally using the broader term antimicrobial resistance (AMR), the UK Government, the European Union, the World Health Organization (WHO) and The World Organisation for Animal Health (OIE) are primarily concerned about the efficacy of **antibiotics** to treat humans and whether the use of **antibiotics** in animals increases the risk of untreatable resistant bacterial infections in humans.

### What is RUMA? (Responsible Use of Medicines in Agriculture Alliance)

RUMA is an alliance of over 26 industry organisations representing every stage of food production from "farm to fork". See <https://www.ruma.org.uk/about/ruma-members/> for full list of current member organisations.

### What does RUMA do?

RUMA aims to promote a co-ordinated and integrated approach to best practice in the use of medicines for farm animals.

### How can RUMA be contacted?

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### Definitions

- **Antibacterial** compounds have a direct action on bacteria, reducing or inhibiting their growth or killing them completely.
- **Antibiotic** is similar to antibacterial, but excludes disinfectants and antiseptics.
- **Antibiotic resistance** is the ability of a micro-organism to grow or survive in the presence of an antibiotic, at therapeutic concentration, that is usually sufficient to inhibit or kill micro-organisms of the same species.
- **Antimicrobial** is the general term for any compound used for treatment or prevention of infections with a direct action on micro-organisms. Antimicrobials include a wide range of compounds - anti-bacterials, anti-virals, anti-fungals and antiprotozoals.
- **Antimicrobial resistance (AMR)** is resistance to any compound with a direct action on micro-organisms used for treatment or prevention of infections.

## 1. ANTIBIOTIC RESISTANCE AND WHY IT MATTERS TO HUMAN AND ANIMAL HEALTH

*Antibiotic resistance is the ability of a micro-organism to grow or survive in the presence of an antibiotic at levels that are usually sufficient to inhibit or kill micro-organisms of the same species.*

### **Why is antibiotic resistance important to human and animal health?**

- The UK's Chief Medical Officer, 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" in her annual report published in March 2013.
- In the May 2016 the 'Review of Antimicrobial Resistance' chaired by Lord Jim O'Neill was published. This has had a significant influence on the UK Government approach to AMR as a One Health issue (<https://amr-review.org/Publications.html>)
- Antibiotic resistance makes bacterial infections and infectious bacterial diseases in humans and animals harder to treat with antibiotics.
- Bacteria have been developing resistance to naturally occurring antibiotics for millions of years. Since the development of medicines to treat bacterial infections, this natural ability of bacteria has led to increasing levels of resistance as bacteria have been challenged and fight to survive.

### **How does antibiotic resistance develop?**

- Antibiotic resistance is complex since resistance factors can be transmitted to the next generation of micro-organisms, and transfer between bacteria of the same or even different species.
- Resistant micro-organisms can spread between species, including from animals to humans and vice versa.
- It is not known exactly how, or to what extent antibiotic use in animals contributes to resistance in humans. Scientific evidence increasingly recognises that the problem of antibiotic resistance in human pathogens comes largely from the use of antibiotics in human medicine. Nevertheless, in the recent JIACRA report, fluoroquinolone resistance in Salmonella and Campylobacter was found to be linked to the consumption of fluoroquinolones in food producing animals.

### **Is antibiotic resistance the same as antimicrobial resistance?**

- No – antibiotic resistance is included within the broader term of antimicrobial resistance.
- Antibiotic resistance relates only to the ability of a bacterium to grow or survive in the presence of an antibiotic, rather than other wider ranging antimicrobial compounds.

### **What's the cause of antibiotic resistance in humans and how can it be controlled?**

- The consensus amongst experts is that the main cause of antibiotic resistance in human pathogens is the overuse and/or inappropriate use of antibiotics in human medicine.
- Inappropriate use of antibiotics could include prescribing antibiotics for viral infections such as flu and cold where they have no effect on the virus, not completing a course of antibiotic treatment, or prescribing the wrong antibiotic for the bacteria involved.
- The threat of increasing resistance to antibiotics is being tackled by various initiatives in UK hospitals and GPs' surgeries, specifically to improve prescribing practices and reduce disease transmission.
- Significant reductions in the rate of antibiotic resistance have been reported, for example in the rate of MRSA infections in hospitals, which has been achieved by strict infection control measures.

### **Can antibiotic use in animals cause antibiotic resistance in humans?**

- There is evidence of transfer of resistant bacteria between animals and people. Whilst it is believed to be uncommon it is more likely to occur where there is close contact between people and animals carrying bacteria. For example, transmissible resistance to the antibiotic colistin was first reported in China in February 2016 (Lancet Infect Dis 2016; 16:161-68). On the basis of the relative levels of resistance in animals and humans, the authors concluded that "it is likely that MCR-1 mediated colistin resistance originated in animals and subsequently spread to people". They noted that China had been one of the world's highest users of colistin in agriculture.
- Although evidence of a direct link between antibiotic use in animals and antibiotic resistance in human pathogens is scarce, all antibiotic use drives antibiotic resistance and so it is right to ensure the responsible use of antibiotics in animals and humans.

## **2. ANTIBIOTIC USE ON UK FARMS**

*Food producing animals, just like people, are susceptible to bacterial infection and disease, whatever the system of farming. Antibiotics are used in farm animals, as they are in people. Effective treatment with antibiotics is sometimes necessary to protect animal health and welfare and, ultimately, food safety and quality.*

### **Why are antibiotics used in UK farming?**

Antibiotics are used in farm animals in the following circumstances.

1. **Therapy** – to treat and cure sick animals.  
Curative treatments, also known as **therapy**, for a sick animal or group of animals, when the diagnosis of disease or infection has been made.
2. **Metaphylaxis** – to control disease spreading in groups of animals where some are already sick.  
Control treatments, sometimes referred to as **metaphylaxis**, for a group of animals after a diagnosis of clinical disease within the group. This aims to prevent the spread of disease to other animals in close contact, and thus at risk, which may already be (sub-clinically) infected. A useful comparison with human medicines would be where a child is diagnosed with meningococcal meningitis necessitating urgent treatment of all other 'in-contact' children.
3. **Prophylaxis** – to prevent sickness or disease developing in a group of healthy animals where a vet has diagnosed there could be a high risk of bacterial infection.  
Preventive treatments, sometimes referred to as **prophylaxis**, for an animal or a group of animals, before clinical signs of disease, to prevent the occurrence of a disease or infection. A useful comparison with human medicine would be where a patient is given antibiotics before surgery to address the increased bacterial challenge during and after the operation. Preventive treatment with antibiotics in animals should:
  - only be applied to animals diagnosed at high risk of bacterial disease on the basis of epidemiological and clinical knowledge from the prescribing vet
  - only occur under prescription by a veterinarian on the basis of epidemiological and clinical knowledge
  - not be applied routinely
  - not be used to compensate for poor hygiene or for inadequate husbandry conditions.

*Note: Highest Priority Critically Important Antibiotics for human treatment should not be used preventatively in animals or as the first line of treatment, unless there is a clear scientific justification to do so.*

### **When are antibiotics used in farming?**

- Under UK and EU animal welfare legislation, farmers are legally required to ensure that animals receive appropriate treatment if they become sick. Removing their ability to do this by appropriate prescription of antibiotics could have a negative effect on animal health and welfare.
- Treating and curing infections in animals with antibiotics is under strict veterinary direction and antibiotics may only be used on a farm if they have been prescribed by a veterinarian. This ensures antibiotics are only used where necessary and in a way that is safe and effective, ensures effective disease control, and protects animal and consequently human health.
- As with all infections, prompt and targeted treatment is essential to prevent unnecessary pain and suffering and animal welfare legislation requires that sick animals receive appropriate treatment.

### **Can antibiotics be used as growth promoters?**

- No. The use of antibiotics for growth promotion is not allowed in the EU. Antibiotic growth promoters have been banned from use in the UK and all other EU countries since 1 January 2006.

### **Can antibiotics be used in all farming systems?**

- Antibiotics are used in all farm production systems, including organic systems.
- In organic systems the use of antibiotics is limited to curative treatments for treating and curing actual infections, they are not normally permitted for the prevention of sickness or disease (metaphylaxis and prophylaxis).

### **How does antibiotic use differ between farming systems?**

- Animals in all systems of farming may be exposed to infection and disease and thus may need to be treated with antibiotics.
- Antibiotics can be used under veterinary supervision and controls, in intensive, extensive, and organic farming systems.
- In organic farming, rules are set to limit the use of antibiotics to situations where alternative treatments such as homeopathic and herbal preparations are considered not to work. Control and preventive treatments (metaphylaxis and prophylaxis) are not normally permitted in organic farming.

### **Do intensive farming systems contribute more to the overall risk of antibiotic resistance than extensive farming systems?**

- For optimal animal health and welfare, good animal husbandry and biosecurity practices are needed in all farming systems, whether these are intensive, extensive, or organic.
- There is no scientific evidence that intensive farming systems contribute more to the overall risk of antibiotic resistance than extensive farming systems.

### **Should targets be set to reduce the amount of antibiotics used on farms?**

- All medicines on farm should be used as little as possible and as much as necessary. Antibiotic use should be reviewed as part of a farm health plan and monitored carefully to encourage responsible use. In the case targets are set, unintended outcomes such as a shift from older but effective to more modern antibiotics that require lower doses by weight should be avoided.
- Reducing use by, for example, withholding necessary treatment, using lower than recommended doses or switching to an inappropriate antibiotic because it has a lower amount of active ingredient per dose is not responsible use. It could encourage the development of antibiotic resistance and compromise animal health and welfare. However, in recognition that there is a wider imperative to curb unnecessary and inappropriate antibiotic use, targets have been developed by leading farmers and veterinary surgeons in each livestock sector as part of RUMA's Targets Task Force initiative (see [www.ruma.org.uk/targets-task-force/](http://www.ruma.org.uk/targets-task-force/)). These targets reflect the unique challenges and opportunities in each sector and continue to drive responsible reduction, refinements or replacements of antibiotics on-farm.

- Good farm management should be adopted to reduce the risk of disease challenge, using medicines only when required and then using them appropriately.

RUMA provides free guidance to farmers and vets on the responsible and effective use of medicines in agriculture. Responsible use of antibiotics on farms means using antibiotics as little as possible and as much as necessary. Regardless of the farming system, the focus for improved animal husbandry should include improved biosecurity practices and on-going vet and farmer training on disease prevention and the responsible use of antibiotics.

### **3. RISKS TO PUBLIC HEALTH FROM ANTIBIOTIC RESISTANCE**

*Antibiotics are important for treating infection and disease and maintaining health for both people and animals. Antibiotic resistance can develop in bacteria infecting both people and animals.*

- Antibiotic resistance is the ability of a bacterium to grow or survive in the presence of an antibiotic at levels that are usually sufficient to inhibit or kill micro-organisms of the same species.
- It is possible for resistant bacteria to pass from animals to humans and vice versa.

#### **What is the current view on antibiotic resistance from UK experts?**

- The UK's Chief Medical Officer Professor Dame Sally Davies, when addressing the All Parliamentary Scientific Committee on 11 June 2013, said "the use of antibiotics in animals is not a massive problem in the UK – and we must work to make sure it doesn't become one".
- It is important that all parties work together to ensure that antibiotics remain effective for the treatment of infection and disease in people and animals, so that when they need to be used, they are available.
- Scientific evidence increasingly recognises that the problem of antibiotic resistance in humans comes largely from the use of antibiotics in human medicine.
- The medical profession is working to improve responsible prescribing and use in people.
- The farming sector needs to take responsible use of antibiotics and other veterinary medicines seriously, to reduce the risks of increased resistance.

#### **Is antibiotic resistance in humans and animals the same?**

- Clinical resistance leading to treatment failures in veterinary medicine occurs, but it is less frequently reported than in human medicine.
- Comparing human and animal resistance levels is difficult because different ways for measuring resistance levels are often used and they are not comparable.
- Harmonised techniques are needed in Europe and worldwide, across animals and people, to allow for meaningful comparisons of antibiotic resistance levels to be made.

### **What are the different measures used in humans and animals?**

- Most reports measure antibiotic resistance in human medicine as the percentage of bacteria that are clinically resistant to one or more antibiotics. This is defined using the clinical breakpoint (CBP), the concentration (mg/L) of an antibiotic which defines whether a species of bacteria is susceptible or resistant to the antibiotic.
- Measurement of antibiotic resistance in veterinary medicine can be based on whether the pathogen causes disease in animals or whether the pathogen causes disease only when transferred to humans.
- Resistance of animal pathogens is also commonly assessed by veterinarians on the basis of appropriate clinical breakpoints
- Resistance of human pathogens in animals is more frequently measured by the percentage of bacteria that are less susceptible to one or more antibiotics at the epidemiological cut off value (ECOFF).
- The ECOFF is a laboratory measurement of reduced susceptibility and is generally set at a lower level than the clinical breakpoint and in those cases treatment with antibiotics would still be effective, even though the ECOFF indicates some reduction in susceptibility.
- ECOFF measures reduced susceptibility, not actual clinical resistance and is therefore different from the clinical breakpoint.
- Measuring resistance levels of human pathogens in animals (using ECOFFs) can lead to resistance levels appearing to be higher than they are when compared to resistance levels in humans, as the scientific methodology is different.<sup>1</sup> Therefore, results cannot be directly compared.

### **What are Highest-Priority Critically Important Antibiotics (HP-CIAs) and why should they be available for use in animals?**

- The current range of antibiotics authorised for use in animals provides a key element in the veterinary surgeon's ability to treat the diseases they encounter.
- This range of antibiotics also includes some considered to be 'highest-priority critically important' (HP-CIAs) for use in treating humans.
- HP-CIAs should remain available for veterinary use since they provide key treatments against animal diseases for which there are currently few or no viable alternatives. The use of HP-CIAs in the veterinary sector is very low, demonstrating that vets only use these products as a last resort, where there is a specific diagnosis and, where possible, when antibiotic susceptibility testing shows there is no alternative treatment option.
- HP-CIAs should not be used preventively or as first line treatment in veterinary medicine unless there is clear scientific justification to do so.<sup>2</sup>
- HP-CIAs reserved for human use should be clearly defined and these definitions should be harmonised between animal and human health authorities and globally. The O'Neill Review on Antimicrobial Resistance refers to the need to

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<sup>1</sup> This difference is highlighted in 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".

<sup>2</sup> An exception for continued use could be as a dry cow treatment to prevent mastitis (in cows' udders) at the end of a milking cycle since scientific evidence shows there is little risk of antibiotic resistance developing in this case.

globally agree upon a harmonised approach to identify those antimicrobials of greatest importance for human health, and whose use in animals represents the greatest risk.

- Currently the UK Government refers in its surveillance reporting (UK Veterinary Antibiotic Resistance and Sales Surveillance Report) to the list of HP-CIAs advised by the European Medicines Agency<sup>3</sup>, i.e. fluoroquinolones, 3rd and 4th generation cephalosporins and colistin should only be used in animals where no other product will be effective for the condition being treated.

#### 4. RESPONSIBLE USE OF ANTIBIOTICS IN FARMING

Like all medicines for people and animals, antibiotics in farming should be used responsibly, which means:

- **Use as little as possible** - farms should be managed so that the risk of disease developing is minimised. Good husbandry practices such as good hygiene, well ventilated sheds, access to clean water, good biosecurity controls and good farm health planning, including appropriate vaccination strategies, will all help to reduce the disease challenge.
- **Use as much as necessary** - when animals become ill they should be treated in accordance with instructions on the label and from the farm's veterinary surgeon.
- Antibiotics should be used only as prescribed by the farm's veterinary surgeon.
- The full course of antibiotic treatment should be given.
- HP-CIAs for human treatment should be used only as a last resort in animals, and should not be used preventively or as first line treatment, unless there is clear scientific justification to do so.

#### How can responsible use of antibiotics be encouraged?

- Antibiotics should only be prescribed by veterinary surgeons.
- A viable network of rural veterinary practices is essential for notifiable disease surveillance and control, and for ensuring that farm animal health and welfare is maintained.
- Companies should be encouraged to develop new antibiotics and alternatives to antibiotics for veterinary use.
- More training, especially Continuing Professional Development (CPD), should be available to vets to help them prescribe antibiotics responsibly and to keep up to date with developments on antibiotic resistance.
- Across the EU, Member States should be encouraged and helped to produce responsible use guidelines relevant to their national farming practices.
- RUMA provided the model for the European Platform for the Responsible Use of Medicines in Animals (EPRUMA) which is ideally placed to help develop future guidelines in the EU.

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[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/582341/1051728-v53-UK-VARSS\\_2015.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/582341/1051728-v53-UK-VARSS_2015.pdf)



## How can irresponsible use of antibiotics be avoided?

- Antibiotic resistant bacteria can transfer from animals to humans and vice versa which could lead to treatment problems: RUMA acknowledges this and promotes the responsible use of antibiotics to reduce this risk.
- Antibiotics can also be used responsibly to prevent disease emerging where a vet has diagnosed a serious threat of bacterial infection in a group of animals. However, such preventive treatment with antibiotics (prophylaxis):
  - should only be applied to animals diagnosed at high risk of bacterial disease
  - should only occur under prescription by a veterinarian on the basis of epidemiological and clinical knowledge
  - should not be applied routinely
  - should not be used to compensate for poor hygiene or for inadequate husbandry conditions.
- Reduction targets for antibiotics must be carefully chosen to reflect the situation in each livestock species and avoid unintended consequences that increase the risk of resistance.
- Reduced dosages or reduced treatment periods to meet reduction targets may result in non-therapeutic levels of antibiotics being used, which in turn could be more likely to encourage resistance development.
- Increased use of the more potent HP-CIAs (meaning less active ingredient is required and less antibiotic is used in crude weight terms) could also encourage irresponsible use of antibiotics.
- These challenges have been addressed by all the major livestock species in the UK by farming and veterinary leaders working together in the RUMA Targets Task Force that delivered species specific targets in the [RUMA Targets Task Force Report 2017](#) at the RUMA conference on 27 October 2017.<sup>4</sup>
- Targets Task Force: One Year On report released November 2018 – downloadable here [RUMA TTF 1 year on – Full Report FINAL](#).

## How can farmers and vets get advice on the responsible use of antibiotics?

- RUMA's guidelines on the responsible use of antibiotics and antimicrobials stress the need for good farm management and disease prevention strategies to minimise the risk of disease. The guidelines are available free at: <https://www.ruma.org.uk/antimicrobials/guidelines/>
- Additional guidance on prescribing for veterinary surgeons is available at [www.bva.org.uk](http://www.bva.org.uk).

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<sup>4</sup> <https://www.ruma.org.uk/wp-content/uploads/2017/10/RUMA-Targets-Task-Force-Report-2017-FINAL.pdf>