Antibiotics play a vital role in both animals and people. As there are only a limited number of antibiotic classes available and as a range of antibiotics is required to treat the many different species of animals that face particular disease threats, some classes of antibiotics are used in both people and animals. Based on the need to use and preserve these medically important antibiotics, there are important ‘One Health’ considerations to take into account when veterinary professionals prescribe such medicines. One consideration is how best to use and preserve ‘Critically Important Antibiotics’ (CIAs). As there is much discussion and conflicting advice about what we mean when we refer to CIAs, this document intends to clarify the meaning of this term from a UK and animal health perspective.

1. The World Health Organisation (WHO) categorises antimicrobials used in human health as ‘critically important’, ‘highly important’ and ‘important’ to human health (1). The critically important antimicrobials are therefore the most important to human health. The WHO CIA antimicrobial group contains products licensed for use in veterinary medicine including aminoglycosides, 3rd and 4th generation cephalosporins, fluoroquinolones, glycopeptides, macrolides, certain penicillins and polymixins.

2. The European medicines regulator – the European Medicines Agency (EMA) - has, on request from the European Commission, assessed the CIAs based on their degree of risk to human health due to antimicrobial resistance development following use in animals. The work, carried out by the Antimicrobial Advice Ad Hoc Expert Group (AMEG), has resulted in the further categorisation of CIAs into risk categories, as shown below (2, 3).

**Category 1: Low or limited risk to public health:** Includes macrolides, certain penicillins and tetracyclines, which are considered to belong to this lower risk category. These antimicrobials should be used with current responsible use practices to keep their risk low.

**Category 2: Higher risk to public health:** Includes antimicrobials for which the risk to public health from veterinary use is only acceptable provided that specific restrictions are placed on their use. This category includes fluoroquinolones, 3rd and 4th generation cephalosporins and, most recently, colistin (4). These antimicrobials should only be used when there are no alternative antimicrobials authorised for the respective target species and indication.
European Medicines Agency (EMA) Antimicrobial Expert Group (AMEG) Classification of WHO Critically Important Antimicrobials (CIAs) based on degree of risk to humans due to antimicrobial resistance development following use in animals

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk to Public Health</th>
<th>Antimicrobials Included</th>
<th>Advice on use</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Authorised CIA’s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Low/limited risk to public health</td>
<td>Narrow spectrum Penicillins, Macrolides, Tetracyclines</td>
<td>General principles of responsible use to be applied</td>
</tr>
<tr>
<td>2</td>
<td>Higher risk to public health</td>
<td>Fluoroquinolones, systemic 3rd/4th generation Cephalosporins, (Aminoglycosides, broad-spectrum Penicillins), Colistin</td>
<td>Restricted to use where there are no alternatives or response to alternatives expected to be poor</td>
</tr>
</tbody>
</table>

3. The UK regulatory agency, the Veterinary Medicines Directorate, recognises and supports the EMA expert view and have stated the following in the 2015 UK Veterinary Antibiotic Resistance and Sales Surveillance Report;

**What are Critically Important Antibiotics (CIAs)?**

Certain antibiotic classes are categorised by the World Health Organisation (WHO) as critically important antibiotics for human use, of which several are designated as ‘highest priority critically important antibiotics’ (HP-CIA). In December 2014, the European Medicines Agency published scientific advice on the risk to humans from antibiotic resistance caused by the use of HP-CIAs in animals. This advice classed macrolides as category 1, where the risk of use in animals to public health is low or limited, whereas fluoroquinolones and 3rd and 4th generation cephalosporins were classified as category 2, where the risk for public health is considered higher. Following discovery of a novel gene conferring resistance to colistin and capable of horizontal transmission (mcr-1) in November 2015, this advice was updated, and the expert group recommended that colistin was moved to category 2, alongside fluoroquinolones and 3rd and 4th generation cephalosporins (5).

4. The assessments made by the independent EMA antimicrobial expert group, the AMEG, which includes human, veterinary and food safety experts, are comprehensive and reviewed when necessary – as demonstrated by the recent reassessment of colistin.

5. The O Neill Review on Antimicrobial Resistance refers to the need globally to agree upon a harmonised approach to identify those antimicrobials of greatest importance for human health, and whose use in animals represents the greatest risk (6).

**In the UK, fluoroquinolones, 3rd and 4th generation cephalosporins and colistin are recognised as the most important of the CIAs, as designated by the European Medicines Agency expert view referred to above (5).**

6. The recommendations provided by the EMA AMEG therefore gives veterinary surgeons an important piece of scientific evidence to factor into their clinical treatment decision making and to responsibly prescribe antibiotics.
Currently, as a full member of the EU until the Brexit process commences, our understanding is that the UK will continue to support the recommendations of the AMEG and the EMA.

References:

2. EMA recommendations on the use of antibiotics in animals: www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp&mid=WC0b01ac058080a585


