Alliance to Save Our Antibiotics response to consultation "Drug resistance – criteria for identifying antimicrobial medicines reserved for treating humans"

23 April 2021

The Alliance to Save Our Antibiotics welcomes this draft document and most aspects of the three criteria that will be used to determine the list of antibiotics that cannot be used in veterinary medicine.

We have two main comments about the approach being suggested. The first relates to one of the criteria being used, the second is a suggestion that the EU that, in addition to banning certain antibiotics from all use in animals, the EU should be considering banning certain antibiotics from use in particular animal species using a similar assessment process.

1. Suggestion for amending criterion C (b)

Criterion C (b) should be amended to read:
"the antimicrobial or group of antimicrobials is used to treat serious, life threatening infections in animals which, if inappropriately treated, would lead to significant morbidity or significant mortality, or would have a major impact on animal welfare or public health, but adequate alternative medicinal products are available for the treatment of those infections in the animal species concerned **or most or all of these infections can be avoided through improved farming practices and animal husbandry**;" [bold added]

Similarly point (7) of the recital of the Delegated Regulation should be amended to read:
"While assessing whether an antimicrobial could be reserved for the treatment of certain infections in humans, it is important to determine whether its absence of use in veterinary medicine would result in significant morbidity or significant mortality or would have a major impact on animal welfare and public health. In the latter case, the availability of adequate alternative medicinal products for the treatment of the diseases concerned in the animals species concerned **or the possibility that the disease could be avoided through improved farming practices or animal husbandry** should be considered" [bold added]

An important weakness of the criterion C is that it does not take into account the possibility of avoiding the use of antibiotics, including antibiotics used as a last-resort in human medicine or those that are particularly important in human medicine, by improving farming practices and animal husbandry to minimise or avoid certain diseases.

Criterion C (b) only considers alternative treatments as an option for avoiding the use of antibiotics that are used to treat serious, life-threatening infections in animals. It does not consider that many of these infections may be avoided through better husbandry.

It is known that certain husbandry practices, some of which unfortunately remain legal in the EU, are associated with much higher levels of disease in farmed animals. Antibiotics, including sometimes last-resort antibiotics in human medicine, are sometimes then used to treat these diseases. The use of particularly important antibiotics, which satisfy criteria A and B, should not be permitted in such circumstances, and therefore criterion C (b) must be amended to refer to improved husbandry as an option for avoiding disease and antibiotic use.

The antibiotic colistin, which is used as a last-resort antibiotic in human medicine for treating certain life-threatening infections, continues to be used in the EU for treating post-weaning diarrhoea in piglets, despite the fact that this incidence of this disease is heavily influenced by husbandry practices. In our view this is a completely unacceptable misuse of an antibiotic which is used as a last-resort in human medicine for treating certain life-threatening infections.

Early weaning of piglets is associated with higher levels of post-weaning diarrhoea. In the EU, the minimum weaning age for piglets, so long as certain conditions are met, is just 21 days. In contrast, in organic farming weaning of piglets is not permitted before 40 days. These different husbandry practices have a major impact on the incidence of post weaning diarrhoea, and on antibiotic use. Recently published data has shown that in Denmark, where antibiotic-data is collected for all farms in the country, average antibiotic use in organic weaner piglets is 15 times lower than for non-organic weaner piglets kept indoors [1].

Similarly, a survey which compared antibiotic use on pig farms in Sweden, Belgium, France and Germany found that average antibiotic use in Swedish weaner piglets was 15 to 30 times lower than in the three other countries, and the difference in antibiotic use has been mainly attributed to the much later weaning on the Swedish pig farms [2][3].

Numerous other husbandry factors can influence disease and antibiotic-use levels – providing a low-stress environment, using low stocking densities, providing access to the outdoors, as well as giving animals appropriate, healthy diets can all contribute to avoiding disease and excessive antibiotic use. Similarly, the use of appropriate, resilient breeds is important, and the use of very fast-growing broilers in intensive broiler farming is linked with higher levels of antibiotic use [4].

It is important to note that countries with lower husbandry standards and higher levels of antibiotic use in livestock tend to have higher levels of antibiotic resistance in their animals. Very high levels of antibiotic resistance can limit treatment options and result in more frequent use of critically important antibiotics, or last-resort antibiotics. Allowing these antibiotics to be used just because husbandry practices are poor is unacceptable.

For example, the Norwegian and Swedish pig industries tend to have much lower antibiotic use than in most of the rest of Europe. This is partly due to their later weaning of piglets and to other better husbandry standards that they use. As a result, Norway and Sweden have much lower levels of antibiotic resistance in their pigs than most of the rest of Europe.

Harmonised European testing showed that, in 2019, 91.2% of E. coli from fattening pigs in Norway were sensitive to all tested antibiotics and just 2.8% were multi-resistant, and in Sweden these figures were 71.3% and 10.9% respectively [5].

Since antibiotic sensitivity remains so widespread in E. coli from pigs in Norway and Sweden, the use of more important antibiotics, such as colistin, fluoroquinolones or modern cephalosporins can be avoided and resistance to these antibiotics in Norwegian and Swedish porcine E. coli was not found in 2019.

In comparison, in Portugal just 3.2% of E. coli from fattening pigs are sensitive to all antibiotics tested, with 74.4% being multi-resistant. This extremely high level of resistance leads to higher use of antibiotics that are last-resort or high-priority critically important in human medicine and as a result resistance to colistin, ciprofloxacin and cefotaxime in the Portuguese porcine E. coli was 8.6%, 26.8% and 5.1% respectively.

Low husbandry standards and high levels of disease are clearly driving farm antibiotic use in many European countries. But the resulting high levels of antibiotic resistance should not then be used as a reason for using last-resort or high-priority critically important antibiotics.

To avoid this happening, criterion C (b) needs to be amended to take account of the possibility of avoiding disease and antibiotic use through better husbandry.

2. The EU should also apply the three criteria on a species-by-species basis

If criterion C (b) is amended as suggested above, the Alliance to Save Our Antibiotics believes the three criteria will provide a good basis for deciding which antibiotics should be banned from all veterinary use.

However, a major weakness of the EU's approach is that it is not considering also applying these criteria to end the use of certain antibiotics in certain animal species.

Under this draft regulation, if an antibiotic is particularly important for protecting the health of one animal species, species A, and there is little evidence that use of the antibiotic in species A is leading to resistance in human infections, but on the other hand there is clear evidence that its use in another animal species, species B, is leading to transmission of resistance to humans and to treatment failures and potentially human deaths because the antibiotic is last-resort treatment or one of the few treatments available for treating life-threatening infections, and the antibiotic is not essential for avoiding mortality and morbidity in species B, then the possibility exists that regulators will decide that the antibiotic should not be banned restricted to human use because of its importance to the health of species A. If this were to happen, no new restrictions would necessarily be introduced on the use of the antibiotic in species B, despite the clear scientific evidence that such use was causing treatment failures for life-threatening infections in humans.

The Alliance to Save Our Antibiotics believes that if an antibiotic meets criterion A, and meets criterion B and C in a particular species, then the use of the antibiotic in that species should be banned.

An example would be the use of fluoroquinolones in poultry, which we believe should be banned.

Fluoroquinolones, unfortunately, are licensed for mass medication in poultry in the EU despite their importance for treating serious food-poisoning infections in humans, and the clear scientific evidence this misuse of these critically important antibiotics has led to some very high levels of resistance in human Campylobacter infections.

According to an ECDC and EFSA report published in February:
"In 2019, very high to extremely high resistance levels to ciprofloxacin were reported in human Campylobacter jejuni isolates from all reporting countries with the exception of Bulgaria, Iceland, Norway and the United Kingdom, where high levels were reported" [5].

And according to an earlier ECDC and EFSA report, this high level of resistance is linked to resistance in poultry:
"Given the high levels of resistance to fluoroquinolones in broilers and the assessment that a large proportion of human campylobacteriosis infections comes from handling, preparation and consumption of broiler meat, this is a compelling example of how AMR in food and animals may impact the availability of effective antimicrobial agents for treating severe human Campylobacter infections" [6].

It is well known that fluoroquinolone use is not essential in poultry, since such use has been banned in the United States since 2005. Fluoroquinolone resistance in human Campylobacter infections in the United States is now far lower than in the EU because of this ban and despite the high use of fluoroquinolones in human medicine in the US.

To minimise treatment failures in human medicine from the misuse of antibiotics in food animals, the three criteria should also be considered on a species by species basis to evaluate whether antibiotics should be removed from use in specific species.

References

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