

NPA BRIEFING



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NPA briefing note on colistin resistance

Background:

- In November 2015 *The Lancet Infectious Diseases* published a report^[1] from China describing the discovery of a transferable gene, *mcr-1*, in *E.coli* from pigs, raw meat and humans. The *mcr-1* gene gives bacteria resistance to colistin.
- Colistin belongs to the class of antibiotics known as polymyxins and is usually used only as a last resort in humans if modern antibiotics are ineffective. However, the increased occurrence of multi-drug resistant infections has meant that colistin is now more important in human medicine.
- Colistin is mainly used in pigs, poultry and veal calves to treat *E. coli* which causes serious disease with potential for high morbidity and mortality. Veterinary products containing colistin are only administered to animals as an oral solution (usually via drinking water) in the UK^[7], not in feed, and the treatment period is for only 3-5 days.
- The *mcr-1* gene has recently been found in bacteria isolated from food-producing animals, food, humans and the environment in several countries worldwide, including the UK^[2,3].
- Nevertheless, the overall prevalence of colistin resistance remains – so far and with some exceptions – low in food and animals in Europe^[4].
- The following describes findings made in England and Wales to date:
 - *E.coli* from three separate pig farms were found to be positive for the *mcr-1* gene. Two were recovered during screening of archived isolates collected from clinical diagnostic investigations. The other was found during screening of samples of intestinal material from pigs collected throughout 2015.
 - **Crucially, the bacteria with the resistance gene were found to be susceptible to many other antibiotics.**
 - Isolates of *E. coli* collected from pigs in England & Wales in 2013 and 2015 as part of government surveillance were also screened and none were found to carry the *mcr-1* gene.
 - Additionally, 24,000 archived bacteria isolated from humans and food were screened. Fifteen isolates were found to carry the colistin resistance gene (twelve *Salmonella* isolates; three *E.coli* isolates).
- The Veterinary Medicines Directorate, who lead on antimicrobial resistance (AMR) policy in Defra, have said these results suggest that *mcr-1* is present in gut bacteria of pigs in the UK, however the precise level is not well defined at this time. **Following these findings the VMD has increased surveillance for colistin resistance.**
- **Public Health England have assessed the risk to human health from *mcr-1* in pigs to be very low.** The Food Standards Agency has advised that the risk from pork that is handled hygienically and cooked thoroughly is very low.

- In light of these recent findings, the European Medicines Agency (EMA) has reviewed its categorisation of colistin, moving it from category 1 to category 2, so that it should only be used when there are no effective alternative antimicrobials from category 1 available for treatment of infection. It is also not allowed to be used for the prevention of disease, only treatment^[4].
- The **Responsible Use of Medicines in Agriculture (RUMA) Alliance**, of which the NPA is a member also announced voluntary restrictions on colistin use in livestock in the UK^[5]. It has been restricted to an antibiotic of last resort and therefore veterinary practitioners will only prescribe it if susceptibility testing shows it is the only effective antibiotic available for treating the sick animals.
- The EMA has also recommended that EU Member States reduce use of colistin to below 5 mg/PCU and ideally below 1mg/PCU. In the UK, use of colistin in animals is already well below 1mg/PCU (Figure 1).

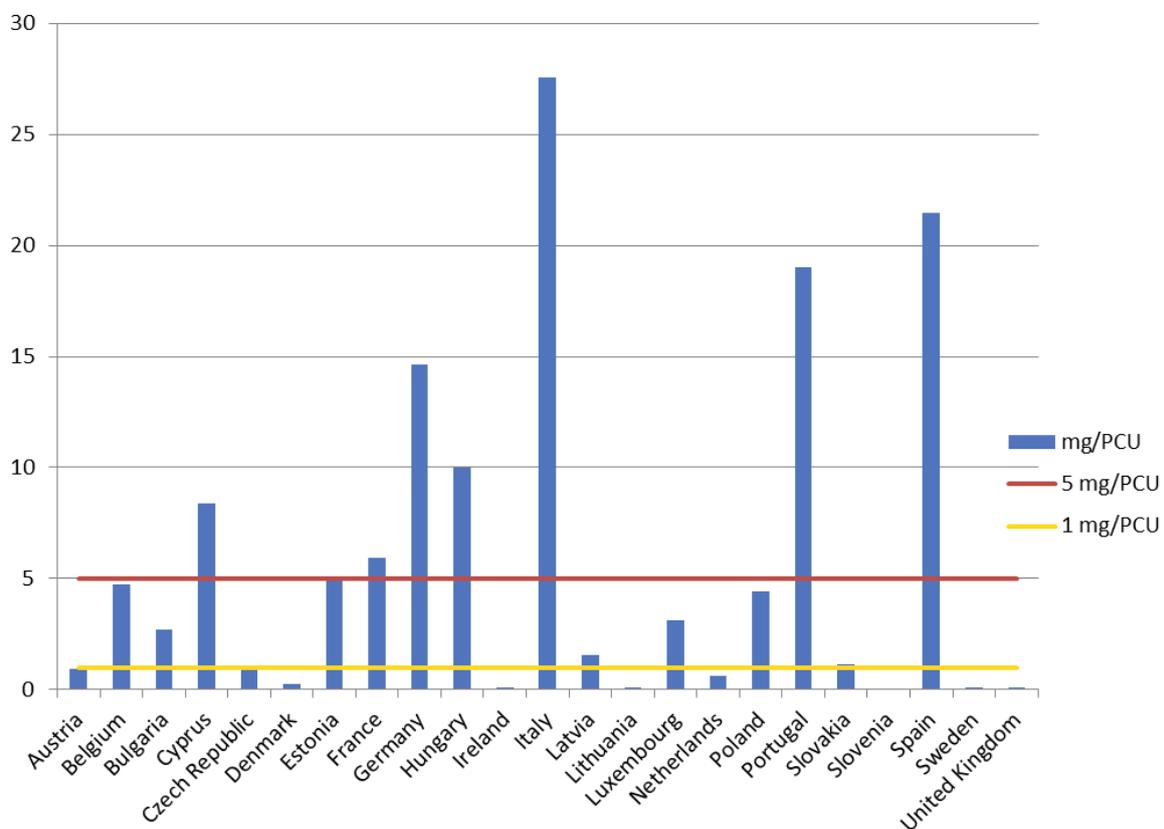


Figure 1 Sales of colistin for use in animals in mg/PCU in 2013 (ESVAC data), including the 5 and 1 mg/PCU levels^[4].

NPA position:

- The finding of colistin resistance in bacteria from pigs in the UK is a concern and the pig industry is committed to preventing further development of resistance to this newly important antibiotic. Antibiotics are a necessary tool for the protection of animal health and welfare and it is in our interest, as well as that of the human medical sector, to ensure that they continue to be effective.
- Despite the use of colistin in veterinary medicine for over 50 years, the level of colistin resistance in European countries remains low and spread of resistance has not been substantial^[4]. However, further work needs to be done to understand how easily this gene is transferred between bacteria to give us a greater understanding of the risk.
- The misuse of antibiotics, including colistin, in human medicine is outside our control. However, NPA is of the position that all sectors who use antibiotics, including the pig industry, have a role to play in ensuring that they are used responsibly. The pig industry recognises antibiotic resistance as a crucially important issue and will continue to engage proactively. For more information about antibiotic use in the pig industry and actions it is undertaking to minimise use, please see our antibiotic use briefing^[6].

References

^[1] Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Liu, Yi-Yun et al., *The Lancet Infectious Diseases*

^[2] <http://www.vettimes.co.uk/news/scientists-find-mcr-1-gene-in-food-and-human-isolates/>

^[3] <http://www.vettimes.co.uk/news/vmd-releases-more-details-of-uk-mcr-1-gene-tests/>

^[4] http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/05/WC500207233.pdf

^[5] <http://www.ruma.org.uk/ruma-announces-voluntary-restrictions-on-colistin-use-in-uk-livestock/>

^[6] [http://www.npauk.org.uk/Pages/Biosecurity/NPA%20briefing%20on%20Antibiotic%20use%20in%20pigs%20-%20External%20\(updated%20May%202016\).pdf](http://www.npauk.org.uk/Pages/Biosecurity/NPA%20briefing%20on%20Antibiotic%20use%20in%20pigs%20-%20External%20(updated%20May%202016).pdf)

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