REDUCING ANTIMICROBIAL RESISTANCE IN FOOD PRODUCTION:

HOW HEALTHCARE PROFESSIONALS CAN HELP

INTRODUCTION

Healthcare institutions across Europe serve a large number of meals to patients, visitors, and staff every day.[1] Their significant purchasing power means that they are well positioned to drive sustainability in the food supply chain and tackle some of the health issues linked to food production. This is especially true of antimicrobial resistance (AMR), which is an increasing threat to human health globally.

AMR occurs when bacteria, viruses, fungi, and parasites develop mechanisms to hinder the effect of antimicrobials designed to treat the infections they cause.[2] Antimicrobial-resistant microorganisms survive and reproduce at the expense of other microorganisms. Whilst this is a natural phenomenon, the overuse and misuse of antimicrobials quickly accelerates the process.

In the EU/EEA, AMR causes an estimated 33,000 deaths per year.[3] Unless further action is taken, AMR could cause 390,000 deaths per year in Europe by 2050 and 10 million deaths globally - more than the expected number of deaths caused by cancer and diabetes combined.[4] Global increases in healthcare costs are also expected, which may range from $300 billion to 1 trillion annually.[5]

The decreased effectiveness of antibiotics (antimicrobials active against bacterial infections) is particularly concerning. In the EU/EEA, nearly 40% of the health burden of AMR is caused by infections from bacteria resistant to last-resort antibiotics, antibiotics used to treat infections resulting from bacteria that are resistant to common antibiotics.[3] When these antibiotics are no longer effective, some infections may be impossible to treat.

The food production sector contributes to this problem. The overuse and misuse of antibiotics in farming is associated with a growing number of resistant bacteria that can spread to humans through direct contact with animals on farms, through the processing, transport, or handling of food animals and food, and through the environment.[6, 7, 8]

Between 2010 and 2030, global antimicrobial consumption in livestock is estimated to increase by 69%, driven by growing demand for livestock products in middle-income countries and the development of large-scale farms.[9] In 2018, 6,431 tonnes of active antimicrobial substances were sold for animal consumption in Europe, and between 2017 and 2030, antimicrobial sales for food production in Europe are projected to increase by around 6.7%. .[10, 11]

This situation is all the more worrying when we consider that the development pipeline of new antibiotics is running dry - almost all new antibiotics brought to market in recent decades are variations of antibiotic classes discovered in the 1980s.[12, 13, 14]

ANTI-MICROBIAL USE IN FOOD PRODUCTION

Antimicrobial overuse and misuse in food production is common in intensive farming practices. This section features examples of antimicrobial overuse in three different species that contribute to the spread of resistant pathogens.

Interventions that reduce antibiotic use in farm animals could decrease the prevalence of antibiotic-resistant bacteria by about 15% and of multidrug-resistant bacteria in animals by 24–32%.[15] In addition, improved hygienic conditions in farms can have a positive effect on animal growth, and prevent widespread disease amongst livestock.[15, 16]

Thanks to recent interventions, between 2011 and 2020, there has been a 43% decrease in overall antimicrobial sales for food production in 25 European countries as reported by the European Medicines Agency (EMA).[17] These interventions include measures that improve animal welfare and reduce stress levels, such as rearing animals in outdoor spaces, feeding them specific diets, introducing longer weaning periods, and lowering stocking density (which can reduce the spread of disease amongst livestock, and therefore the need for antimicrobials).[7]

However, important differences remain in the use of antimicrobials by country. Of the 25 European countries providing data for 2011-2020, 19 reported a decrease of more than 5% in the sales of veterinary antimicrobial medicinal products, whereas four countries reported an increase of more than 5%. The remaining two countries noted a minor increase or decrease (below 5%) in overall sales. The EMA reports that overall, the sales of antimicrobials for veterinary use decreased by 60% in some countries, and suggests that there is still room for improvement in Europe.[17]

In 2020, 14% of antimicrobial veterinary medicinal product sales in 31 European countries were classes of antimicrobials identified as 'critically important for human medicine' (CIAs) by the World Health Organization (WHO). Nearly 90% of these medicines were antimicrobials typically used for animal group treatment.[17]

POULTRY

The routine use of antimicrobials in poultry farms is often aimed at improving meat production by preventing potential disease.[18] Farmers use them because they are a cheap and easy solution against infectious diseases. Furthermore, veterinarians cannot visit farms on a regular basis and farmers lack training in terms of antimicrobial use in their farms.[19]

Each year, 7.2 billion broilers, i.e. chickens intended only for meat production, are slaughtered in the EU.[20] Around 90% of these are reared in intensive farming systems, where fast-growing strains of birds are prioritised over slower growing ones.[21, 22] These fast-growing breeds require more antibiotics, which suggests that they are more exposed to infections.[22]

Evidence shows an association between the consumption of fluoroquinolones, an antibiotic class frequently used in poultry, in food-producing animals and resistance to fluoroquinolones in *E.Coli, Salmonella, and Campylobacter jejuni bacteria* in humans. This is particularly concerning as countries with a high consumption of fluoroquinolones, such as ciprofloxacin, amongst food-producing animals tend to also have a high consumption in humans.[7] In Spain, between 2001-2016, resistance to ciprofloxacin in *E.Coli* samples increased from 17% to 91%.[23]

According to a study analysing samples from the three largest EU poultry companies, one in every two samples tested positive for simple or multi-resistance to various antibiotics.[24]

Good animal husbandry (quality of feed and water, good ventilation, efficient inspection of animals), effective biosecurity measures (buying from disease-free suppliers, keeping hygienic conditions), and vaccination can prevent infectious disease, and therefore reduce the need of antimicrobials.[25]

PIGS

The process of weaning is stressful for pigs. It can be the source of intestinal and immune system dysfunctions that can affect their health, growth, and feed intake.[26, 27] Weaning is the change from milk consumption to other sources of feed intake, which naturally happens when the piglet is aged between 12 and 17 weeks. [28, 29]

Many farmers, however, reduce the weaning period to improve the economic efficiency of their farms, increasing the use of medication.[30] The sow herd can take on more pigs per sow per year if the weaning period is, for example, 17 days instead of 28.[31]

Early weaning may eventually result in neonatal diarrhoea in piglets, which is associated with the proliferation of *E.Coli* bacteria in the intestine.[32] To treat this bacteria in piglets, the antibiotic colistin is widely used.[32] The common use of colistin in pigs has allowed this species to become reservoirs for the spread and development of resistance to this antibiotic.[33]

Antimicrobial use for group treatment and the prevention of neonatal diarrhoea in piglets is a common practice in Europe due to early weaning. Pigs can be treated individually with antibiotics, but it is more common that pigs receive group treatment either via water or feed.[34]

Piglets raised in France, Belgium, and Germany consume between 20-30 times more antibiotics than piglets raised in Sweden, where piglets have on average 10-12 days longer weaning periods than piglets from other EU countries.[35]

CALVES

In calf breeding, mixing young calves from different herds contributes to spreading infection, which leads to group treatment with antibiotics. Respiratory diseases and diseases leading to diarrhoea are the most common infections.[34] Beef cattle are often affected by Bovine Respiratory Disease (BRD), which is the most common illness during the fattening period in Europe, and accounts for the majority of antimicrobials used in cattle worldwide.[36, 37] In Denmark, for example, 79% of antimicrobials used to treat veal calves were used to treat BRD.[38]

If BRD was eradicated, the productivity of the beef sector would increase by 4.7-5.5%.[39] BRD control has therefore become one of the main reasons for antimicrobial use when it comes to calves.[40] Metaphylaxis* and prophylaxis** are major drivers of antimicrobial consumption, yet the use of mass medication provides inconsistent control of BRD and remains a concern in terms of the emergence of AMR.[41, 42]

The way in which calves are raised might affect their exposure to BRD and their consumption of antimicrobials. One study from Belgium showed that calves raised indoors in intensive production systems received 25 times more antibiotic treatments than beef cattle reared outdoors and with lower intensity.[43]

* **Metaphylaxis**: administration of antibiotics to some members of the herd after a diagnosis in one of the animals to prevent any further infection.

** **Prophylaxis**: treatment of animals or a herd as a preventive measure, with no sign of infection.

THE DUTCH MODEL

In 2008, the Netherlands started applying a new policy framework to reduce antimicrobial use in farming.[44] Between 2009 and 2016, the use of antibiotics in livestock decreased by more than 64%, with many farmers increasing both profits and productivity.[45] Good practices included: improving transparency in recording antibiotic use on farms and in the prescription patterns of veterinarians, strengthening the role of veterinarians, measures to improve animal health, and the promotion of a prudent use of antimicrobials.[46] This model also prioritised the use of antibiotics in animals that are less important for human health, under the supervision of veterinarians.

THE CASE OF COLISTIN

Colistin is an antimicrobial from the polymyxin class discovered in the late 1940s. Whilst its use in human health was originally very restricted due to its toxicity, colistin is now widely used as a last-resort antibiotic to treat infections caused by gram-negative bacteria that are resistant to carbapenems.

In 2016, polymyxins were added to the WHO's List of Critically Important Antimicrobials (CIAs) because of the increasing use of colistin to treat serious infections in humans in many parts of the world, the discovery of the mcr-1 and mcr-2 genes that confer transmissible resistance to colistin, and the spread of colistin-resistant bacteria via the food chain.[47]

COLISTIN IN THE EU

Colistin has been used in veterinary medicine across Europe since the 1950s.[48] In Europe, sales of polymyxins for animal use declined by nearly 70% between 2011 and 2018, but the consumption of colistin in animals still vastly outweighed consumption in humans in 2017.[11]

In 2020, polymyxins accounted for 2.8% of total antimicrobial sales for food-producing animals in Europe, 99% of which was sold in a format suitable for group treatment, i.e. premixes, oral powder, and oral solutions. The consumption of polymyxins as a percentage of total antimicrobial consumption varies across Europe and ranges from 0% in countries such as Finland, Iceland, or Norway to 8.8% in Germany. Furthermore, 100% of the polymyxins sold in Germany were in formats suitable for group treatment.[17]

The EU is still behind countries such as the USA and Canada, which have never allowed its use in farming, or India and Argentina, which have banned colistin in food production.[49, 50, 51]

In the EU, polymyxins are not considered a "Category A" antibiotic by the European Medicines Agency (EMA), a category including antibiotic (sub)classes that cannot be used in veterinary medicine but are authorised in human health.

WHERE DOES RESISTANCE TO COLISTIN COME FROM?

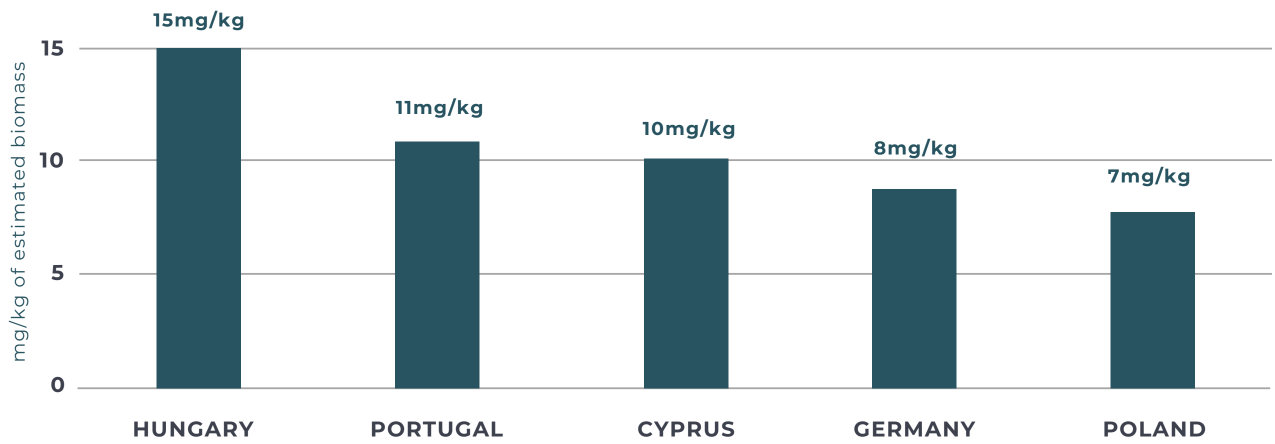
It is difficult to track the origin of colistin-resistant bacteria. The most likely scenario is that the colistin-resistant gene mcr-1 was first found in animals and then quickly spread to humans.[52] The mechanism through which the mcr-1 gene confers resistance to colistin was first discovered in China in November 2015 and samples of this gene were quickly found in more than 30 countries.[53, 54]

Colistin-resistant bacteria are spreading around the world through the trade of food animals and food but also through infected humans.[53, 55] The situation is especially worrying in Southern Europe, where increasing carbapenem resistance has led doctors to start using colistin more frequently to treat bacteria resistant to carbapenems.[7]

In one Greek hospital, colistin resistance rates rose from 0% in 2007 to 8.1% in 2008 and to 24.3% in 2009.[56] Likewise, in Italy, there has been a steep rise in colistin resistance in *K. Pneumoniae* bacteria, from 1-2% in 2006 to 33% in 2009.[49]

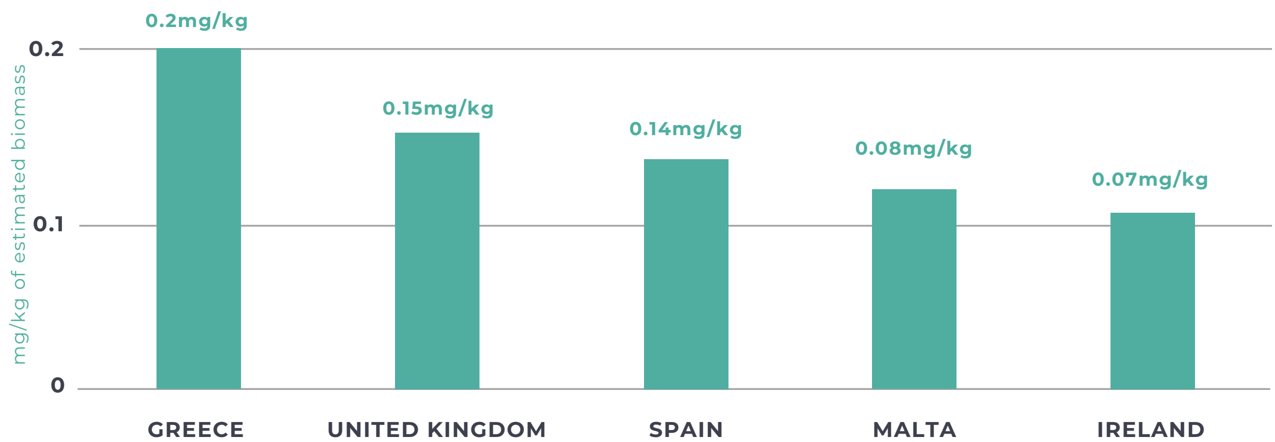
Consumption of colistin in animals and humans in 2017 in Europe[7]

Top consumption of colistin in animals (rounded figures):



(EMA, ECDC, EFSA, 2021)

Top consumption of colistin in humans (rounded figures):



(EMA, ECDC, EFSA, 2021)

EU REGULATION ON VETERINARY MEDICINAL PRODUCTS

On 28 January 2022, a new regulation on veterinary medicinal products will enter into force in the EU[57]. This new regulation is one of the pillars of the EU Action Plan against AMR and is in line with the EU Farm to Fork Strategy target to reduce overall EU sales of antimicrobials for farmed animals and in aquaculture by 50% by 2030.[58]

The new regulation only allows the preventive use of antimicrobials in exceptional cases. Metaphylaxis will not be considered as an exceptional case under the new regulation. Similarly, prophylaxis will also not be permitted.

The regulation mandates the European Commission to designate antimicrobials or groups of antimicrobials reserved for the treatment of certain infections in humans. The list will apply to food both produced and imported into the EU, establishing an important international standard.

The new regulation on veterinary medicinal products will be the latest in a string of EU policy initiatives aimed at reducing AMR in food production, in recognition of this growing health threat.

Recent initiatives taken by the EU to reduce AMR in food production.

2006 – Ban on the use of antibiotics for growth promotion

2011 – 2011-2016 Action Plan against the rising threats from AMR

2013 – Designation of AMR as a serious cross-border health threat, requiring member states to monitor and report on the correct use of such medicines

2017 – European One Health Action plan against AMR

2022 – New Veterinary Medicinal Products Regulation

WHAT CAN HEALTHCARE PROFESSIONALS DO?

The healthcare sector can play a key role in driving sustainability and fostering responsible antimicrobial use in food production.

1. BECOME AN ANTIMICROBIAL STEWARD

Healthcare professionals are well placed to influence policies within their institutions to leverage healthcare's purchasing power so that it can drive meaningful change. Sustainable food procurement policies can facilitate the shift to supply chains that protect human health against the growing threat of AMR.

Here are four recommendations for healthcare professionals to implement effective advocacy strategies in healthcare:

a. **Find allies:** Find colleagues interested in reducing your healthcare institution's contribution to AMR and form an action group in which you can discuss the scope of your future actions.

b. **Define your goals:** Draft a set of concrete actions that your institution could carry out and provide a list of easy-to-measure indicators (see page 17).

c. **Meet the right people:** Identify key bodies/groups within your institution that can help you reach the objectives established by your action group. This could be the management board, the procurement team, sustainability team, or any other department with decision-making authority. Share your personal experiences of treating patients with antibiotic-resistant bacteria to help procurement staff understand the gravity of the situation. You can follow the guidelines developed by Clinician Comprehensive Antibiotic Stewardship (CCCAS) Collaborative to drive action through storytelling.

d. **Build momentum around AMR:** Raise awareness about this issue amongst other colleagues. Try to identify key dates for advocacy activities such as events, thematic coffee/lunch breaks, internal communications and posters (such as the ones developed for the World Antimicrobial Awareness Week), in order to raise awareness and keep your colleagues informed about the activities and objectives of the group.

KEY DATES

7 JUNE	17 SEPTEMBER	16 OCTOBER	18 NOVEMBER	18-24 NOVEMBER
World Food Safety Day	World Patient Safety Day	World Food Day	European Antibiotic Awareness Day	World Antimicrobial Awareness Week

CONCRETE ACTIONS FOR HEALTHCARE INSTITUTIONS:

For more detailed recommendations check out the antimicrobial stewardship through food animal agriculture toolkit module

Track your institutions' meat consumption: Establish the total cost and volume of all the products purchased, and check which products come from organic producers. Organic farming standards don't allow the routine use of antibiotics, which makes organic products a more responsible option.[5]

Identify potential alternative producers: Check if your organisation's current producers provide meat raised without routine antibiotics. If not, identify other sources and make a list of potential alternative suppliers.

Start with small changes: Identify products that might imply minimal cost implications to start a transition to antibiotic-free meat. Products with a higher cost may take longer to transition to.

Create a roadmap: Once you have a list of alternative products, create a roadmap for the introduction of these products. The roadmap should include a timeline and the cost implications of each new product.

Demonstrate the business case for action: Treating antibiotic resistant bacteria has a cost for your healthcare facility (extended hospital stays, antibiotic prescriptions, treatments for arising complications, etc.). Where possible, try to quantify this impact and demonstrate why switching to antibiotic-free meat is more cost-effective for your institution.

2. ENCOURAGE YOUR ORGANISATION TO JOIN HCWH EUROPE'S HEALTHCARE MARKET TRANSFORMATION NETWORK

HCWH Europe has established a working group on responsible antimicrobial use in food production within the Healthcare Market Transformation Network. This network is open to members of Global Green & Healthy Hospitals, and leverages the healthcare sector's purchasing power to drive policies and markets towards sustainable products and services.

The overarching goal of this working group is to increase demand from the European healthcare sector for food produced with responsible antimicrobial use to address the growing threat of AMR.

The working group will:

- **Exchange best practices on food procurement amongst European healthcare facilities**
- **Develop a set of standard procurement criteria on antimicrobial use in food served in European hospitals based on the EU's Green Public Procurement criteria**
- **Engage with healthcare facilities across Europe to endorse these procurement criteria**

We are looking for food procurement staff within healthcare facilities/systems and healthcare professionals with a particular interest in antimicrobial use in food production.

If you or your colleagues are interested in taking part in this working group, please complete this form.

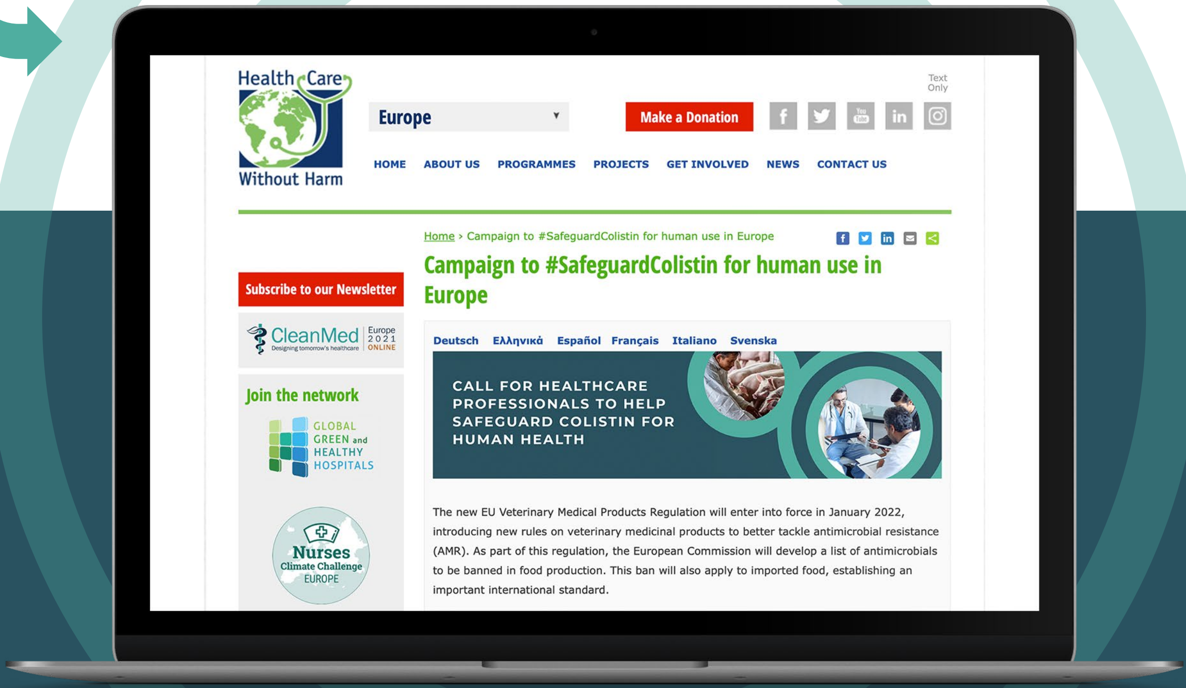
3. SUPPORT AN EU BAN ON COLISTIN IN FOOD PRODUCTION

The EU Veterinary Medical Products Regulation mandates the European Commission to develop a list of antimicrobials to be banned in food production. This ban will also apply to imported food, establishing an important international standard.

Despite its importance for human health, colistin is still used in veterinary medicine across Europe. It is crucial that colistin is on this list in order to safeguard this vital medicine in the fight against AMR.

Join other European healthcare professionals to stop the spread of AMR and sign the petition calling on the European Commission to ban colistin in EU food production and meat imports.

SIGN THE PETITION!



SHARE IT WITH YOUR COLLEAGUES!

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