ICFAW Position on the Use of Antimicrobials in Livestock Production

The World Health Organisation has warned of *"a post-antibiotic era, in which many common infections will no longer have a cure and once again, kill unabated."*

Summary

Globally approximately half of current antimicrobial production is used in agriculture, to promote growth and prevent disease as well as to treat sick animals.

The excessive recourse to antimicrobials in human medicine is the major cause of antimicrobial resistance in humans. However there is also a clear link between antimicrobial consumption in farm animals and antimicrobial resistance in humans.

The therapeutic treatment of individual sick animals with antimicrobials is often essential. It relieves suffering and returns them to health and economic production. Restrictions on the use of antimicrobials for growth promotion or routine disease prevention should not inhibit the use of antimicrobials for genuine therapeutic treatment.

ICFAW believes that the use of antimicrobials for growth promotion should be phased out worldwide. This is no longer permitted in the EU and the U.S. has prohibited the use of "medically important" antimicrobials for growth promotion.

ICFAW believes that routine prophylaxis and metaphylaxis in groups of animals should be brought to an end.

Routine preventive use of antimicrobials is primarily a feature of intensive livestock production. Antimicrobials are routinely given to whole herds or flocks via their feed or water to prevent the diseases that would otherwise be inevitable where animals are confined in overcrowded, stressful conditions and are bred and managed for maximum yield. These conditions compromise their health and immune responses, and encourage disease to develop and spread.

Disease should be prevented by good hygiene and biosecurity, good husbandry and enriched (not barren) housing rather than by reliance on regular preventive use of antimicrobials. Ending routine mass prophylaxis would – rightly - not prevent individual non-routine prophylactic use of antimicrobials - for example when an animal needs antimicrobials following a difficult birth, an operation or an injury.

ICFAW believes that health-orientated systems for rearing animals should be developed in which good health is inherent within the system rather than being propped up by

routine use of antimicrobials. Such systems would avoid the factors that routinely predispose animals to disease. In particular, they would avoid overcrowding, excessive group size and severe confinement. They would reduce stress, for example by enabling animals to perform their positive natural behaviours and avoiding painful procedures. Early weaning in pigs would be ended. Mixing would be avoided and long distance transport and the sale of live animals at livestock markets or auctions would be minimised. Such systems would move away from genetic selection for high production levels where these involve an increased risk of immunological problems and pathologies.

Detailed Position

Contribution of use of antimicrobials in farming to antimicrobial resistance

The excessive recourse to antimicrobials in human medicine is the major cause of antimicrobial resistance in humans.[i] However, both the World Health Organisation (WHO) and the European Medicines Agency stress that the regular prophylactic use of antimicrobials in farming contributes to the transfer of resistant bacteria to people.[ii] [iii]

The WHO has stressed that the use of antimicrobials in food animal production contributes to increased resistance to antimicrobials and that, worldwide, approximately half of current antibiotic production is used in agriculture, to promote growth and prevent disease as well as to treat sick animals. The WHO adds: "With such massive use, those drug resistant microbes generated in animals can be later transferred to humans".[iv] Crucially, these microbes are not just resistant to antimicrobials used in farming but may also develop resistance to related antimicrobials used to treat serious human disease, as is currently the case for entire classes of substances, including last-resort antimicrobials such as colistin, carbapenems, or linezolid..

The WHO states: "Extensive research into mechanisms of antimicrobial resistance, including the important role of horizontal gene transfer of antimicrobial resistance determinants, supports the conclusion that using antimicrobials in food producing animals selects for antimicrobial resistance in bacteria isolated from food producing animals, which then spread among food-producing animals, into their environment, and to humans. Furthermore, the systematic reviews concluded that broad restrictions covering all antimicrobial classes appear to be more effective in reducing antimicrobial resistance compared to narrow restrictions of one antimicrobial class or drug, even though there are examples of marked reductions in antimicrobial resistance following restriction of a single antimicrobial."[v]

The O'Neill *Review on Antimicrobial Resistance* established by the UK Government reports a clear link in the scientific literature between antimicrobial consumption in farm animals and resistance in humans. It calls for a substantial reduction in antimicrobial use in farming as an important aspect of the strategy for combating antimicrobial resistance.[vi] WHO Guidelines recommend: "an overall reduction in use of all classes of medically important antimicrobials in food-producing animals".[vii]

Scientific research shows that for some bacterial infections, such as Campylobacter and Salmonella, farm antimicrobial use is the principal cause of resistance in human infections.[viii] For other infections, like E. coli and enterococcal infections, farm antimicrobial use contributes significantly to the human resistance problem.[ix] [x]

Use of antimicrobials in livestock production

Antimicrobials are used in farming for the following purposes:

Growth promotion: This is no longer permitted in the EU and the U.S. has prohibited the use of "medically important" antimicrobials for growth promotion. However, antimicrobials continue to be used for growth promotion in many parts of the world. ICFAW believes that the use of antimicrobials for growth promotion should be phased out worldwide as the efficacy of antimicrobials in human medicine should not be undermined by their use as growth stimulants

in farming. The WHO recommends "complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion".[xi] It adds that any increased costs of animal production associated with complete restriction of growth promotion use of antimicrobials "appear to be relatively small or non-existent".

Treatment: The therapeutic treatment of individual sick animals with antimicrobials is often essential. It relieves suffering and returns them to good health and economic production. Restrictions on the use of antimicrobials for growth promotion or routine disease prevention should not inhibit the use of antimicrobials for genuine therapeutic treatment.

As prophylaxis to prevent disease: In intensive production, animals are kept in stressful, overcrowded conditions and are bred and managed for maximum yield (to grow faster or to produce more meat, milk, eggs or offspring). These conditions can compromise their health and their immune responses and encourage the development and spread of infectious disease. In order to prevent this, antimicrobials are frequently given to whole herds or flocks of intensively farmed animals via their feed or water.

Routine preventive use of antimicrobials is primarily a feature of intensive livestock production

The European Medicines Agency has said "In animal production systems with high density of animals or poor biosecurity, development and spread of infectious diseases is favoured, which leads more frequently to antimicrobial treatment and prevention of those diseases. This provides favourable conditions for selection, spread and persistence of antimicrobial-resistant bacteria. Some of these bacteria are capable of causing infections in animals and if zoonotic also in humans. Bacteria of animal origin can also be a source for transmission of resistance genes to human and animal pathogens".[xii]

The O'Neill *Review on Antimicrobial Resistance* states that prophylactic use is "particularly prevalent in intensive agriculture, where animals are kept in confined conditions":[xiii]

The WHO states growing demand for meat "especially when met by intensive farming practices, contributes to the massive use of antibiotics in livestock production".[xiv]

The UN Food and Agriculture Organisation states: "the prevalence of resistance in the agricultural sector is generally higher in animal species reared under intensive production systems".[xv] A White Paper produced by the World Economic Forum states: "the increase in livestock intensification has also meant a rise in the use of antibiotics." [xvi]

The link between intensive farming and high levels of antimicrobials use is highlighted by the fact that the Veterinary Medicines Directorate's data show that around 83% of UK farm antimicrobial use is in pigs and poultry, the two most intensively farmed species.[xvii] Danish Ministry of Agriculture data show that antimicrobial use is much greater in intensive pigs than in organic pigs.[xviii]

A Belgian study reports that antimicrobial use in intensively farmed veal calves is much higher than in more extensively raised beef cattle.[xix] A recent Joint Scientific Opinion by the European Medicines Agency and the European Food Safety Authority states that in intensive veal production "there is comingling of young, recently transported, highly stressed calves from multiple farms ... In this industry, the disease risk is high, in particular bovine respiratory disease and there is very high on-farm use of antimicrobial agents."

Two types of preventive use: prophylactic and metaphylactic

Prophylaxis is the giving of antimicrobials to a group of animals to prevent disease even though none of them are infected and no clinical disease is present. Metaphylaxis is when some animals in a group are infected and antimicrobials are given both to the ill animals and to others in the group to prevent spread of the disease within the group.

Need to end routine prophylactic and metaphylactic use of antimicrobials
In 2018 Agriculture Ministers produced a Communiqué at the 10th Global Forum on Food and Agriculture stating that they aim "to strive to restrict the use of antibiotics in veterinary medicine to therapeutic uses alone."[xx]

There is a widespread consensus that routine prophylactic use of antimicrobials should be brought to an end. The European Commission's 2015 *Guidelines for the prudent use of antimicrobials in veterinary medicine* state that "routine prophylaxis must be avoided".[xxi]

A Joint Scientific Opinion published in 2017 by the European Medicines Agency (EMA) and the European Food Safety Authority (EFSA) states "there should be an aim to phase out preventive use of antimicrobials, except in exceptional circumstances."[xxii]

The Federation of Veterinarians of Europe states: "Routine use of antibiotics as prophylaxis should be phased out and, in a longer time perspective, completely come to an end. Disease prevention must be based on proper husbandry practices and we should move away from the use of antibiotics against expected bacterial infections at certain points in time of the life of food animals".[xxiii]

The WHO recommends "complete restriction of use of all classes of medically important antimicrobials in food-producing animals for prevention of infectious diseases that have not yet been clinically diagnosed". The WHO adds: "the potential undesirable consequences associated with complete restriction of use of antimicrobials for the prevention of infectious diseases that have not yet been clinically diagnosed in food-producing animals (e.g. adverse effects on animal health and welfare) appear to be relatively small."

The metaphylactic use of antimicrobials in a one-off situation may be necessary to prevent the spread of a disease. However, regular metaphylactic use in group after group indicates that something is wrong with the system. The farmer must take steps to ensure that regular metaphylactic use does not continue but is replaced by disease prevention through improved husbandry, housing and biosecurity. Indeed, the European Commission states in its 2015 Guidelines: "Antimicrobial metaphylaxis should never be used in place of good management practices".

The Joint EMA/EFSA Scientific Opinion states that "there should be an aim at national and farm level to reduce and refine the use of metaphylaxis". It adds: "Metaphylaxis should not be used systematically if the underlying risk factors could be controlled by recognised alternative measures (e.g. vaccination, nutrition, hygiene)."

ICFAW believes that routine prophylaxis and metaphylaxis in groups of animals should be brought to an end. This includes the use of antimicrobials not used in human medicine, i.e. ionophores (including ionophore coccidiostats). Disease should be prevented by good hygiene and biosecurity, good husbandry and enriched (not barren) housing that enables expression of natural behaviours. Reliance on regular preventive use of antimicrobials (including ionophores) should not be relied upon to address the consequences of suboptimal housing and management conditions.

Ending routine prophylaxis would – rightly - not prevent non-routine prophylactic use – for example when an animal needs antimicrobials following a difficult birth, an operation or an injury.

OIE
The OIE is playing a leading role in addressing antimicrobial resistance. Its *Terrestrial Animal Health Code* provides detailed guidance on the responsible and prudent use of antimicrobials.

The OIE played a significant role in developing the WHO Global Action Plan on Antimicrobial Resistance adopted in 2015.[xxiv] This highlights the importance of reducing the use of antimicrobials in farming. The OIE is a member of the Interagency Coordination Group on Antimicrobial Resistance established by the UN Secretary-General.

The OIE has produced a strategy and recommendations for controlling antimicrobial resistance. ***ICFAW urges the OIE to give greater prominence in these documents to the important role of higher animal welfare standards in reducing disease and hence the need for regular antimicrobial use.***

ICFAW believes the curriculum for veterinary students must include a clear understanding of when the use of antimicrobials is appropriate in livestock farming and of the alternatives that should replace routine preventive use of antimicrobials.

Preventing disease without regular prophylactic use of antimicrobials: Developing health-orientated systems for rearing of animals

There is broad agreement that improved husbandry would reduce the risk of disease. The Federation of Veterinarians of Europe states: "a positive association can be seen often between good animal welfare and reduced antibiotic use. Animals which are well cared for and appropriately housed, will be less prone to infections and will need less antibiotics. In other words, ***the more successful the actions aiming at improving animal health and welfare are, the more successful will be the attempts to reduce the use of antibiotics and to curb bacterial resistance in food animals.***" (emphasis present in the original)

The Joint EMA/EFSA Scientific Opinion's recommended options include "improving husbandry and management procedures for disease prevention and control; rethinking livestock production systems to reduce inherent disease risk". It states: "measures must be implemented that improve animal health and welfare and thereby reduce the need for antimicrobials in the first place."

The Joint Opinion examines the factors needed to create more resilient animals that are less susceptible to disease. It states that these include reducing the level of stress resulting from factors such as heat, cold, crowding, restraint, mixing, early weaning, feed restriction, insufficient bedding, lack of enrichment and noise. It adds: "crowding and restraint put pressure on animals". Many of these factors are most typically found in intensive livestock systems. It concludes: "On-farm stressors interfere with the normal behaviour of the animals and have been shown to alter the immune system of animals and susceptibility to diseases."

The Joint Opinion highlights the "need to rethink those particular farming systems which place much reliance on antimicrobial use". It states: "In some farming systems, much reliance is placed on the routine use of antimicrobials for disease prevention or for the treatment of avoidable outbreaks of disease, such that these systems would be unsustainable in the absence of antimicrobials. The stress associated with intensive, indoor, large scale production may lead to an increased risk of livestock contracting disease." It recommends: "Farming systems with heavy antimicrobial use should be critically reviewed, to determine whether/how such systems could sustainably reduce the use of on-farm antimicrobials. If a sustainable reduction in the use of on-farm antimicrobials is not achievable, these systems ideally [should] be phased out."

The *Lancet Infectious Diseases Commission* has stressed that instead of relying on routine use of antimicrobials, we need to develop "health-orientated systems for rearing of animals".[xxv] In such systems good health would be integral to the system rather than being propped up by routine use of antimicrobials. This approach would build good health and strong immunity by (see Figure 1):

avoiding overcrowding: research shows that high densities are a risk factor for the spread and development of infectious disease; such densities can allow rapid selection and

amplification of pathogens;[xxvi] [xxvii] [xxviii] The European Commission's prudent use guidelines highlight the need to "reduce the density of the farm animal population" saying "this is believed to be a major risk factor in the emergence and spread of infections".

reducing stress: stress tends to impair immune competence, making animals more susceptible to disease.[xxix] The Joint EMA/EFSA Scientific Opinion states that the following steps contribute to reducing stress: the provision of proper enrichment, ensuring thermal comfort, proper animal handling, and avoiding feed restrictions. The Joint Opinion points out that pregnant sows and broiler breeders are feed restricted.

enabling animals to perform positive natural behaviours: inability to engage in certain natural behaviours is a major source of stress in intensive systems;[xxx]

ending the early weaning of pigs: this is stressful due to premature removal from the sow, change in diets, mixing with unfamiliar pigs and being moved to a new environment.[xxxi] Pigs should not be weaned until they have gained immunological and nutritional independence from the sow. Danish Ministry of Agriculture data show that antimicrobial use is 20 times greater in intensive weaners than in organic pigs which are weaned at a substantially older age. Pigs should at the earliest be weaned at 28 days of age and preferably later;[xxxii]

avoiding excessive group size: The O' Neill *Review* states: "large numbers of animals living in close proximity ... can act as a reservoir of resistance and accelerate its spread. There are often many opportunities in intensive farming environments for drug-resistant bacteria to be transferred between, for example, thousands of chickens being reared in the same indoor enclosure";[xxxiii]

minimising mixing: Mixing is stressful and can result in the introduction of disease.[xxxiv] Therefore, new animals entering the farm must be quarantined before being introduced to the resident animals;

maintaining good air quality: poor air quality and inadequate ventilation are risk factors for respiratory disease which, if combined with poor hygiene, can represent a significant threat to the health of the animals;[xxxv]

encouraging a move away from genetic selection for high production levels: in some cases these appear to involve an increased risk of immunological problems and pathologies;[xxxvi]

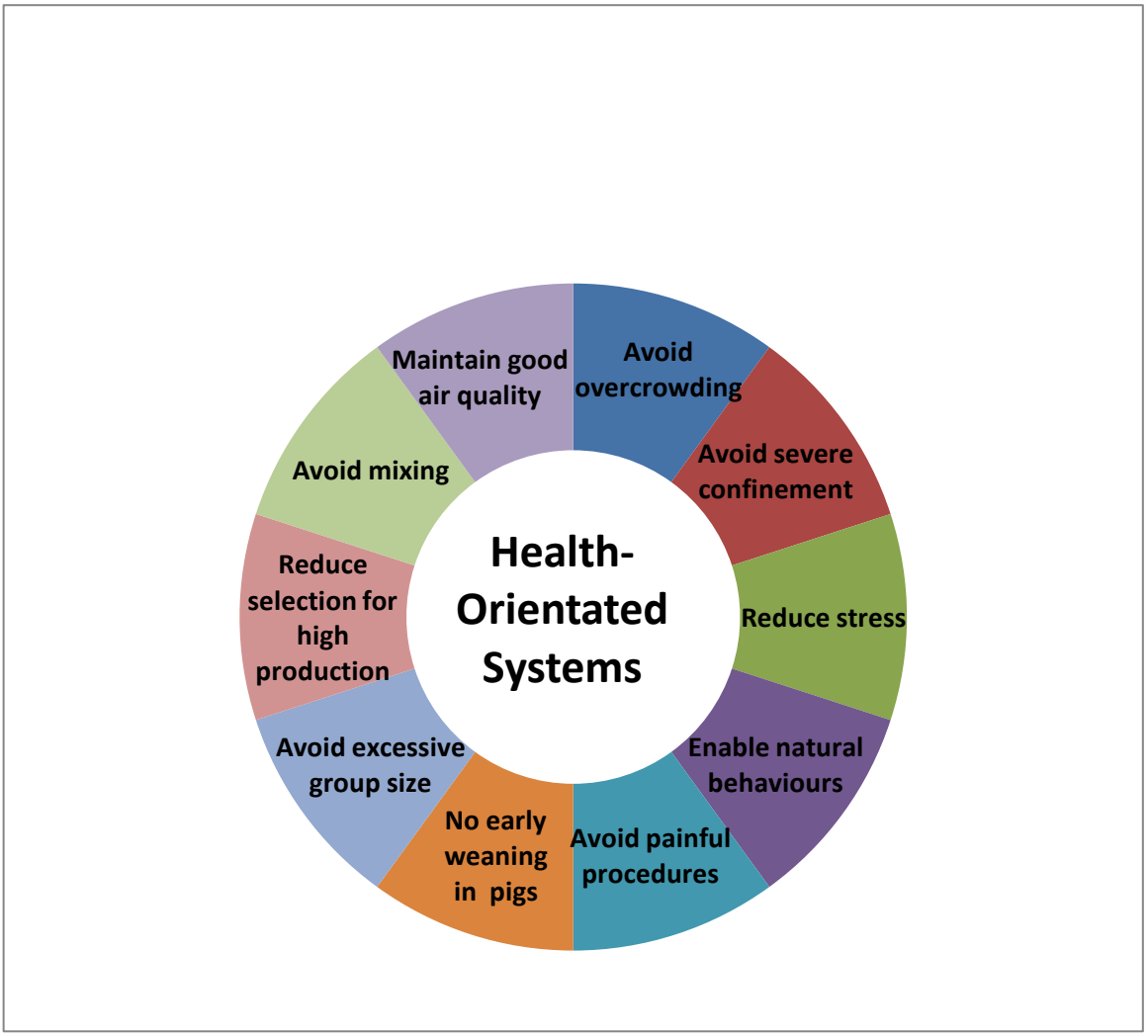
minimising transport: EFSA has concluded that the "transport of animals is considered a major risk for the spread of infectious animal diseases".[xxxvii] It recommends: "In order to reduce the risk of transport-associated disease outbreaks, strategies should be developed to reduce the volume of transport, and long distance transport of animals for finishing or slaughter (e.g. by the transport of carcasses and food products) or reducing journey time (e.g. by slaughtering animals as close as possible to the site of production)."

avoiding use of markets: The Joint EMA/EFSA Scientific Opinion states: "live animal distribution hubs, such as markets, offer the opportunity for pathogen transmission between animals from different farms. For this reason, these hubs should be avoided where possible".

Such health-orientated systems would bring the additional benefit of having much greater potential for delivering good welfare outcomes than intensive systems.

Figure 1

Health-Orientated Systems for Rearing Animals



Reporting of antimicrobial usage

ICFAW supports the collection and monitoring of antimicrobial (including ionophore) usage by all livestock sectors (e.g. as proposed by the OIE in Chapter 6.8 of the Terrestrial Animal Health Code and Chapter 6.3 of the Aquatic Animal Health Code). This information should be available to the public in order to provide transparency to consumers while at the same time allowing the various livestock sectors to demonstrate commitment to the responsible and prudent use of antimicrobials. All livestock sectors should have an antimicrobial stewardship plan in place (reviewed and updated yearly) to demonstrate and assist with responsible and prudent use. The stewardship plan should be an instrument to achieving a phase out of prophylactic antimicrobial use in favour of a focus on optimising the animals' environment, on good animal handling and appropriate management practices. At the same time, surveillance and public reporting of antimicrobial resistance is needed to monitor the effect of antimicrobial reduction on prevalence of antimicrobial resistance across all livestock sectors.

Use of critically important antimicrobials

The WHO has produced a list of those antimicrobials that are critically important for human health.[xxxviii] These include flouroquinolones, 3rd and 4th generation cephalosporins and polymyxins (e.g.colistin). ICFAW believes that all group treatment using critically important antimicrobials and all preventive use of these antimicrobials must be phased out. Critically important antimicrobials should only be used to treat individual, sick animals where the causative organism has been established and sensitivity testing, or the results of recent sensitivity testing, shows that no other antimicrobials are likely to work.

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[ii] http://www.ema.europa.eu/docs/en_GB/document_library/Public_statement/2009/10/WC500005152.pdf

[iii] http://www.who.int/mediacentre/news/releases/2011/whd_20110406/en/

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[v] World Health Organisation, 2017. WHO guidelines on use of medically important antimicrobials in food-producing animals. http://www.who.int/foodsafety/areas_work/antimicrobial-resistance/cia_guidelines/en/

[vi] http://amr-review.org/sites/default/files/Antimicrobials%20in%20agriculture%20and%20the%20environment%20-%20Reducing%20unnecessary%20use%20and%20waste.pdf

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