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COMMITTEE ON AGRICULTURE

SUB-COMMITTEE ON LIVESTOCK

First Session

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Alternative feed practices to promote responsible use of antimicrobials

Executive Summary

Antimicrobial growth promoters (AGPs) have been used extensively since the 1940s as part of high external input-dependent livestock systems. Many of the substances used as AGPs are used also for veterinary medical purposes in animals and are classified as medical important antimicrobials for human health by the World Health Organization (WHO). As a result, concerns have arisen about the potential risk for the selection of resistant microbial populations and the transfer of resistant bacteria between animals and humans.

The current understanding of the economic benefits of AGP use under good husbandry practices, and the increasing insight into advanced feeding practices, enable the replacement of AGP use in livestock production, thereby implementing the responsible and prudent use of antimicrobials which is a milestone in the One Health Strategic Action Plan.[1]

The use of AGPs classified as medically important can be phased out and eventually completely avoided without long-term adverse effect on livestock health and productivity, if adequate hygiene, nutrition (including functional feed additives), welfare and other husbandry measures are implemented. The adoption of such measures requires action on several levels, including in legislative frameworks, education and the capacity development of producers. International collaboration and collective action are required to share knowledge and experiences and develop guidance on replacing the use of AGPs in livestock production.

[1] FAO. 2011. *One Health: Food and Agriculture Organization of the United Nations Strategic Action Plan*. Rome. https://www.fao.org/3/al868e/al868e.pdf

Suggested action by the Sub-Committee

The Sub-Committee is invited to recommend COAG to:

- invite FAO to monitor national policy and legislation on the use, phasing out or ban of AGPs in livestock production, and collect data on the impact of these measures on the use of AGPs, animal health, welfare and productivity;
- recommend FAO to conduct an inventory of alternative feeding practices to replace the use of AGPs and develop and disseminate knowledge on these alternative feeding practices; and
- invite FAO to facilitate a Member-driven process to discuss and reach consensus on the development of a non-binding guidance instrument (e.g. a voluntary code of conduct or voluntary guidelines) to support Members to replace progressively the use of AGPs, while maintaining the health, welfare and productivity of livestock.

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I. Introduction

1. Antimicrobial resistance (AMR) is one of the biggest threats to public health and food security and safety. Misuse and/or unnecessary use of antimicrobials in humans, animals and plants is accelerating the development of AMR. AMR affects not only animal and human health but also the economic sustainability of the livestock sector, due to economic losses and missed market and trade opportunities.

2. With the growing awareness of the risk of AMR, many countries have developed AMR national action plans, established stewardship campaigns and implemented policies to safeguard the appropriate use of antimicrobials in humans, animals and plants.

3. In 2015, the FAO Conference adopted Resolution 4/2015 on Antimicrobial Resistance,[2] requesting FAO to "actively support and provide capacity building as appropriate, in collaboration with other relevant partners, sustainable production systems taking into account the social, economic and environmental dimensions that prevent diseases through good animal (aquatic and terrestrial) husbandry management and practices, as well as good plant production management and practices, as an important means to combat antimicrobial resistance", and to "support implementation of the Global

[2] FAO. 2016. *The FAO Action Plan on Antimicrobial Resistance, 2016–2020.* Rome. https://www.fao.org/3/i5996e/i5996e.pdf

Action Plan on Antimicrobial Resistance".[3] Subsequently, FAO developed its Action Plan on Antimicrobial Resistance, the current version of which covers the 2021–2025 period.[4]

4. In November 2021, the Codex Alimentarius Commission adopted the *Revised Code of Practice* to minimize and contain foodborne AMR which establishes, in its principles 12 and 13, that the responsible and prudent use of antimicrobial agents does not include the use for growth promotion of antimicrobial agents that are considered medically important, and that medically important antimicrobial agents should only be used for veterinary medical use and phytosanitary use (treatment, control/metaphylaxis or prevention/prophylaxis of disease).[5]

5. In response to the COAG, which at its 27th Session encouraged FAO to explore alternative ingredients to replace AGPs,[6] this document provides an overview on AGP use in livestock production and the related consequences, presents feeding practices that may contribute to replacing the use and requirement of AGPs, and collective actions needed for the adoption of these feeding practices.

II. Use of AGPs in livestock

A. Use and effects of AGPs

6. AGPs comprise a range of antimicrobial agents administered to animals only to increase the rate of weight gain or the efficiency of feed utilization, and are not a chemically defined class of pharmaceutical compounds. They were first introduced into livestock diets in 1946. The higher production which was observed subsequently resulted in the market introduction of antimicrobials from different classes, such as glycolipids, orthosomycin, polypeptides, macrolides and ionophores. Some of these drugs are exclusively approved for use in animals, while others are included in the World Health Organization (WHO)'s list of medically important antimicrobials for human health. Their introduction was closely related to the development of high input-dependent production systems and considered as a measure to improve livestock health and in particular feed utilization and daily weight gain, two important economic parameters. These desirable effects were observed especially in poultry and pig production.

7. National and global data on the quantities of AGPs used in livestock production are lacking. Several barriers to collecting data on antimicrobials, and more specifically on the quantities of AGPs used, have been reported.[7] One of these barriers is that AGPs were licensed as feed additives (purchased in over-the-counter sales), for which a registry of use is not mandatory.

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[3] World Health Organization (WHO). 2015. Antimicrobial resistance: draft global action plan on antimicrobial resistance, report by the Secretariat. A68/20. 27 March 2015. https://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_20-en.pdf; WHO. 2015. Antimicrobial resistance: draft global action plan on antimicrobial resistance, report by the Secretariat: corrigendum. A68/20 Corr. 1. 21 May 2015. https://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_20Corr1-en.pdf

[4] FAO. 2021. The FAO Action Plan on Antimicrobial Resistance 2021–2025 Rome. https://www.fao.org/3/cb5545en/cb5545en.pdf

[5] FAO and WHO. 2021. Joint FAO/WHO Food Standards Programme: Codex Alimentarius Commission forty-fourth session, 8-13 November 2021. https://www.fao.org/fao-who-codexalimentarius/sh-proxy/es/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-702-80%252FReport%252FFinal%252FREP21_EXEC1e.pdf

[6] FAO. 2021. Conference, forty-second session: report of the 27th session of the Committee on Agriculture (28 September – 2 October 2020). https://www.fao.org/3/cb3902en/cb3902en.pdf

[7] World Organisation for Animal Health. 2021. *OIE Annual Report on Antimicrobial Agents Intended for Use in Animals: Better Understanding of the Global Situation* [online]. 5th Report. Paris, France. [Cited 13 December 2021]. https://www.oie.int/app/uploads/2021/05/a-fifth-annual-report-amr.pdf

8. Despite their broad use, an understanding of the actual mechanisms of the action of AGPs remains incomplete. The major effects observed in livestock have been modifications of the intestinal microbiota and intestinal wall. Other observations have included the stabilization of the intestinal microbiome during dietary changes, the reduction of virulence of entero-pathogens and reduced intestinal inflammation. The improved tolerance to enteric (i.e. *Clostridium perfringens* and *Escherichia coli*) and other zoonotic (i.e. *Salmonella* and *Campylobacter spp.*) pathogens were additional beneficial effects associated with the use of AGPs.

9. As early as 1969, the Swann Report raised concerns about the large-scale use of antibiotics and the risk for selection of multidrug-resistant bacterial strains in animals and the environment.[8] These concerns resulted in the voluntary withdrawal of AGPs from the market, and since the 1980s AGPs have been gradually phased out, many being banned in Canada, the United States of America and the European Union. More recently, Brazil and China endorsed the precautionary withdrawal and ban of some AGPs.

10. A special class of antimicrobials are the ionophores (monensin, salinomycin, lasalocid and narasin), one of the most successful classes of drugs for the prevention of coccidiosis, a challenging disease in poultry, especially in large flocks. These drugs are currently not approved for systemic use in human medicine, and they are not included in the WHO list of critically important antimicrobials. Due to their modulating effect on the intestinal microbiota in poultry and ruminants (cattle, sheep), ionophores have also been classified as AGPs. In the European Union, where other AGPs have been phased out, the use of ionophores as feed additives has continued to be permitted and regulated as a special functional group for the prevention of coccidiosis.

B. Impact of withdrawing AGPs from the livestock sector

11. Various national studies from countries where the withdrawal or ban of AGPs was enforced (such as Denmark, the Netherlands, Switzerland and the United States of America) revealed that these actions did not result in adverse effects on animal health, welfare or production parameters (e.g. mortality, weight gain, feed conversion ratio), but had only a minor effect on short-term economic parameters.

12. Assessing the economic benefits of AGPs on a global scale is a challenge due to the scarcity of data on AGP use, animal health and economic record keeping.

13. Despite the use of AGPs for almost 70 years, the general impact on livestock productivity can hardly be estimated, as the response is highly variable according to the species, the age of the animals, their genetic potential and the specific hygiene and management conditions. Studies conducted before the 1980s reported an improvement in the growth rate and feed efficiency of pigs, poultry and cattle fed antimicrobials at subtherapeutic levels as high as 15 percent. Studies conducted in Denmark, Sweden and the United States of America after the year 2000 pointed to more limited effects, with less than 1 percent or no statistically significant improvement, except for piglet nurseries in which a 5 percent improvement in growth rate was reported. Recent meta-analyses conducted by Brazilian researchers using data from 42 923 pigs (from 103 experiments) and 121 643 broilers (from 183 experiments) showed that the withdrawal of AGPs resulted in lower weight gain and higher feed costs per animal, but the study also indicated a high level of uncertainty in interpretation as the data were not harmonized for livestock genetics, feed regimens and husbandry conditions. In many of these recent studies, the cost of the administration of AGPs is higher than the marginal economic gains in production.

[8] Swann, M.M. 1969. *Report of Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine*. London, UK, Her Majesty's Stationary Office.

14. An explanation of the results reported above is that the loss of production efficiency associated with eliminating the use of AGPs for livestock may be less important or minimal in systems where hygiene, welfare, feeding and production practices are optimized. Therefore, countries with less optimized production systems could observe larger productivity and economic effects from the use of AGPs. The cost of investing in improved practices and their indirect benefits are difficult to estimate, but potentially significant.

III. Replacing AGPs by advanced nutrition and feeding practices

15. This section introduces technical and regulatory animal nutrition and feeding options, including the use of non-antimicrobial drug feed additives, for replacing AGPs use without long-term adverse effects on livestock health, welfare and productivity. In this and the following section, "feed additives" refer to non-antimicrobial drug feed additives.

16. Good nutrition allows the expression of the genetic potential of animals for different traits, including resistance to disease or stress, growth, milk or egg production and reproductive functions. These depend on the availability of sufficient (preferably local) feed resources around the year, the genetic makeup of the animals, climatic and disease conditions and husbandry practices.

17. Livestock nutrition programmes are supported by diverse classes of feed additives, which have already been developed, marketed and used in daily practice. Many of these functional additives are based on traditional fermentation techniques (prebiotics, probiotics and synbiotics) and preservation technologies (organic acids). Other feed additives, such as phytochemicals, have their roots in traditional health practices and ethno-veterinary medicine. Evaluating locally available feed ingredients and traditional remedies based on herbal products abundantly available in the local environment should be integrated into the feeding strategy to reduce the need for the use of AGPs in livestock.

18. Good nutrition also supports the critical functions required for a healthy gastrointestinal tract, host defence and health. Various feeding practices can be used to reduce the presence of potentially harmful contaminants (e.g. pathogenic bacteria and natural toxins such as mycotoxins) and anti-nutritional factors in feed and water. Such practices include:

- Ensuring drinking water quality. The consumption of water of appropriate quality is a prerequisite for animal health. Regular control of the quality, supply and accessibility of water, and regular sanitation of water storage and delivery systems using disinfecting agents, are important measures to keep animals healthy. However, this could prove a challenge in regions with water shortages or high levels of water pollution.
- Ensuring feed safety and quality. Measures to ensure feed safety and quality include: minimizing the presence of microbiological, chemical and physical hazards; ensuring appropriate levels of available protein, energy and other nutrients and micronutrients to meet the requirements of the animal and ensure productivity; and ensuring appropriate physical characteristics such as particle size and pellet durability and hardness. Risk management in relation to the safety of feed and feed ingredients is an essential part of good feed production and manufacturing practices.
- Precision feeding. Knowledge of the nutritional requirements of species and breeds, and their specific needs at different life phases, has advanced feeding regimes, furthering sustainable production level over the entire lifespan. Milestones in advancing feeding practices include the increasing availability and use of high-quality proteins, vitamins, chelated minerals, feed preservatives and enzymes such as phytases, which all improve feed utilization. While these practices are proven to be effective at the producer level, their success partly depends on the safety and quality of feed and feed ingredients, which vary in nutrient and digestible energy content. In many countries, the availability of feed and feed ingredients of sufficient quality at every time of the year is an increasing concern. Agricultural practices, feed processing

(mixing and pelleting) and the level of education of animal nutritionists and producers are key determinants of successful animal nutrition programmes.

- Feed additives. These are intentionally added ingredients not normally consumed as feed by themselves, whether or not they have nutritional value, which affects the characteristics of feed or livestock products. Diverse classes of feed additives have been developed, marketed and used in livestock practices. The total market value was estimated at USD 38 billion in 2021 and was expected to reach USD 50 billion by 2026. These comprise prebiotics, probiotics, synbiotics, organic acids and phytogenic compounds. A wide range of feed additives can be recommended to foster gastrointestinal and overall health, even under physiological or environmental stressful conditions such as weaning and regrouping, heat stress, undesirable anti-nutritional factors and contaminants such as toxins. Such feed additives are promoted based on their effect on gut health, thereby improving feed utilization, the gut-associated immune system and resilience to infectious diseases. While AGPs aim to stabilize the intestinal microbiota, a similar result can be achieved with non-antimicrobial compounds, which balance the microbiome and stimulate digestive enzymes and nutrient transport across a functional intestinal barrier. An improvement of intestinal health directly results in an improvement of the immune competence of an animal, and hence overall resilience against infectious diseases. Improving gut health increases feed efficiency and in turn growth rate and productivity over the entire lifespan in all livestock species. Therefore, feed additives can not only replace AGP use in the improvement of gut health and immune competence, but can also gradually reduce the need of antimicrobials for veterinary medical purposes. However, the efficacy and consistency of many feed additives can vary, and are affected by feed composition, animal health and welfare, management practices and the physical and social environment.

IV. Requirements for the adoption of sustainable feeding practices

19. Feed legislation in many countries does not adequately recognize the impact of nutrition on gastrointestinal health and overall animal health and welfare. Recognition of the prophylactic effects of feed additives used in animal health should further contribute towards reducing AMR.

20. A hindrance to a broad implementation of the above-mentioned practices is the additional cost potentially generated for producers, especially small-scale producers. Traditional AGPs are often cheaper, easy to access (in over-the-counter sales) and use, and are regarded as being effective under poor hygienic and nutritional conditions. In addition, regulatory frameworks securing good husbandry and feed safety practices are often lacking or not adequately enforced.

21. Raising awareness on available low-cost feeding practices and affordable proven technologies is therefore required. This should be coupled with joint efforts, by competent authorities, private sector, intergovernmental organizations and financial institutions, to address the above-mentioned obstacles.

V. Collective actions for replacing AGPs

22. Various feeding practices can be used as building blocks or tools to achieve good animal health and productivity, while simultaneously replacing AGPs and reducing overall antimicrobial use.

23. For livestock producers and feed manufacturers, it can be quite challenging to choose the most effective solution. Decisions to use certain feed additives are often based on the perceived effectiveness, credibility of the supplier, costs versus expected benefits and their own experiences. Compiling an international registry of these (locally) known products, and establishing criteria for the evaluation and safe use of such traditional products and processes, can foster the generation of more evidence on their cost-effectiveness for upscaled adoption. Sharing this knowledge will improve not only animal health, welfare and productivity, but will eventually facilitate more sustainable agricultural practices through the efficient use of local feed resources.

24. To encourage the rapid adoption of best feeding practices, and in recognition of the importance of animal nutrition for animal health and welfare, regulatory authorities may have to revise their current legislation on the health claims of feed ingredients and additives.

25. The replacement of AGPs may remain an economic challenge for countries with limited feed availability and inadequate local feed supplies. Support to Members' efforts to eliminate the use of AGPs, while maintaining good animal health, welfare and productivity, is needed.

26. Subsequently, the Sub-Committee is encouraged to discuss the following:

- how to foster knowledge on cost-effective feeding practices, research on additional feed additives, and assessment of the safety of such compounds;
- how to make an inventory of and share knowledge on best feeding practices that improve animal health and productivity and can be applied to replace the use of AGPs and decrease the need to use antimicrobials;
- how to tailor this knowledge to the conditions of specific livestock production systems and countries;
- how to monitor policy and legislative measures on the current use, phasing out strategies, banning of or other restrictions on the use of AGPs and their impact on animal health, welfare and productivity;
- how to facilitate discussions among Members and stakeholders to reach consensus regarding the possibility of developing a non-binding guidance instrument to support countries to replace progressively the use of AGPs, while maintaining animal health, welfare and productivity.