Title: Antimicrobial use in supplemental livestock feed and the efficacy and effects of alternative supplements

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INTRODUCTION

Antimicrobials, which include antibiotics, antifungals, and antivirals, are added to livestock feed around the world to promote animal growth, weight gain, and health and to increase farm productivity[1,2,3,4]. Livestock are also becoming increasingly susceptible to diseases which is thought to be caused by stress associated with poor living conditions[2,5] and premature weening[5], increasing the demand for antimicrobials in agriculture. Alongside this demand in developed countries is now a demand in developing countries. Countries, like Brazil, Russia, India, China, and South Africa are shifting toward intensive livestock production systems to meet the rise in demand for high-quality protein and fats[1,2,5]. Data shows that the global biomass for animals raised for food exceeds the global biomass of humans[1]. With it, the global use of antimicrobials in supplemental livestock feed is increasing[1,2,5]. This increase in global livestock production improves food security in low- and middle-income countries[1,2,5] and can improve the lives or rural farmers with increased revenue[2,5]. In high-income countries, like the United States, antimicrobial use in supplemental livestock feed is decreasing[1,4,6,7] and many nations are banning it's use for non-medical purposes[1,2,4,5,8]. The misuse of antimicrobials in supplemental livestock feed for the promotion of animal growth and weight gain, as well as improved production, is

increasing global antimicrobial resistant pathogens[1,2,4,5,8,9,10] and ultimately making antimicrobials less effective for human use[1,6,10]. Antimicrobial resistance is a recognized growing global threat[1,5,6,10] and public health concern[1,2,4,5,6,8,9,10]. Despite this, and the bans placed on agricultural antimicrobial use, in high-income nations there is still high demand for agricultural antimicrobials[1,6,7]. In the United States, antimicrobial use for food animals is estimated to account for nearly 80% of the nation's annual antimicrobial consumption[1]. This looming global threat is only one drawback of antimicrobial use for livestock production and health. For example, antibiotics, one form of antimicrobial, can be toxic to animals and have varying efficacy due to their inherent inability to target specific bacteria, thereby harming beneficial microbiota[10]. On a larger scale, the application of antimicrobials in feed and water pollutes water reservoirs and soil creating adverse biogeochemical and ecological effects[1,9]. **Given the consequences of overusing antimicrobials, what are the most effective and sustainable alternatives for livestock and how cost effective are they for farmers in developing nations?**

DISCUSSION

Probiotics

Probiotics, beneficial live microorganisms, are widely studied as an alternative to antimicrobials in agriculture. Given that probiotics are non-toxic and non-pathogenic, they have not been shown to have a negative impact on the environment[2,4,5,9,10]. In fact, these beneficial microorganisms are shown to have a positive impact on livestock health[2,4], to promote weight gain[2,4,5], and may even improve the flavor (lightness, yellowness, and redness) of chicken meat[5]. The most effective probiotics are spore bearing - promoting their longevity in the body, have heat stability, and have the ability to survive in a low pH environment, such as in the stomach[4,5,10]. Several *Bacillus*

species were shown to lower the serum cholesterol levels in chickens as well as relieving oxidative stress and providing antioxidants[5]. Commonly, probiotics are shown to enhance nutrient absorption, improving overall health[3,4,5]. One studied showed that the addition of probiotics in hen feed increased egg production in comparison to those without any supplements[4]. This study demonstrates increased production associated with probiotic supplements. Another study tested the use of a probiotic, called RE3™, as supplemental livestock feed on Guineafowls, a common and important food animal in Ghana and other countries in Africa. They found that Guineafowls who were fed this probiotic showed weight gain in comparison to Guineafowls who were not given supplements, likely due to increased ability to absorb nutrients and a pathogen free gut environment which allows the breakdown of otherwise discarded complex Non-Starch Polysaccharides. This study also showed that the cost of raising Guineafowls supplemented probiotics was less expensive than for Guineafowls not supplemented which is hugely due to the reduction in need for medicine. The gross revenue associated with these Guineafowls was also increased due to their increased weight and quality and the reduced overall cost of raising[2]. This study demonstrates that probiotics, which are widely available and affordable globally[2], can increase livestock weight and quality while also increasing overall profits. More research is needed on the widescale use of probiotics, such as in intensive livestock production, to determine whether this is a general trend and a feasible solution for farmers globally as they increase production to meet consumer needs.

Plants

Plants can be a beneficial supplement for livestock in many forms such as in plant extract or in their natural state. As an extract, plants have been shown to improve nutrient absorption, promote growth, and improve overall health of pigs as well as promoting herd immunity. Plants

also have natural antioxidants and pharmaceutical effects; by some measures plant extract can be regarded as an appropriate antibiotic substitute[3]. Plant extracts are widely available globally and a cost-benefit analysis should be performed to better understand how this method would financially impact farmers in developing nations. A highly technological plant alternative to antimicrobials is using CRISPR, genetic alteration, technology to produce antibodies in plants. This alternative allows for industrial scale production of hand-selected antibodies. This technology is fast, inexpensive, and safe. Antibodies can be designed to withstand low pH and digestive enzymes, reducing the quantity needed to be effective[5]. Low cost and easy access to this technology could benefit farmers in developing countries while allowing them to meet demand with increased production. This promotes the idea that this technology could be a viable option for combating increasing global antimicrobial resistance. Ethics and the potential for unexpected negative ecological impacts should be examined when considering the use and expansion of this technology.

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