ROADMAP TO PHASE OUT NON-THERAPEUTIC ANTIBIOTIC USE AND CRITICALLY IMPORTANT ANTIBIOTICS IN FOOD-ANIMALS IN ZAMBIA

January 2020

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This report presents a roadmap to phase out non-therapeutic use of antibiotics and critically important antibiotics in food-animals in Zambia. It is an outcome of a workshop organized jointly by the national Antimicrobial Resistance Coordinating Committee (AMRCC) through the Zambia National Public Health Institute (ZNPHI) and the Centre for Science and Environment (CSE), India. ZNPHI and CSE would like to thank all experts from Zambia who contributed to the development of this report. The list of experts is provided at the end of this report.

About ZNPHI

ZNPHI (http://znphi.co.zm/), a technical arm under the Ministry of Health, is a public health centre of excellence that addresses all major public health concerns in Zambia. ZNPHI seeks to improve health of all Zambians through coordinating priority public health and health security activities and resources; leveraging strong partnerships at the international, national and sub-national levels; generating and analysing scientific evidence for advocacy, policies and programmes; and prioritizing public health functions. It serves as co-Secretariat to the national AMRCC with the Department of Veterinary Services under the Ministry of Fisheries and Livestock, and is responsible for coordinating the implementation of Zambia's Multi-sectoral National Action Plan on Antimicrobial Resistance.

About CSE

CSE (www.cseindia.org), India, is a non-profit public interest research and advocacy organization working on issues of public health, environment and development in India and global South. The Food Safety and Toxins team at CSE has been working to address the problem of antimicrobial resistance, particularly the animal and environmental aspects of it.

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Foreword

Zambia has joined the growing global movement to fight the threat of Antimicrobial Resistance (AMR). The country has formulated a 10-year National Action Plan (NAP) as the framework for a coherent and coordinated approach to addressing AMR in all sectors and at all levels.

The misuse and overuse of antibiotics in food-animal production is widely recognized as a key driver of AMR in humans who ultimately consume the animals and animal products. As a developing country, Zambia has not been spared from the challenge of unregulated use of suboptimal doses of antibiotics for non-therapeutic purposes such as growth promotion and mass disease prevention (prophylaxis). This is generally more rampant among small scale and emerging farmers, whose survival crucially depends on maximizing production and minimizing losses. This routine exposure of antibiotics to animals in sub-optimal doses drives the emergence, selection and dissemination of resistant bacteria, further amplifying the burden of AMR. Several studies in Zambia have demonstrated the emergence of resistance in bacteria isolated from food-animals. Several initiatives to address this malpractice are under development, including legal provisions to be enforced by regulatory authorities. For instance, a statutory instrument (SI) is under formulation to regulate and limit the use of particular classes of medically important antimicrobials in animals.

To augment and harmonize this and other efforts, the national Antimicrobial Resistance Coordinating Committee (AMRCC) in partnership with the Centre for Science and Environment (CSE) convened a workshop of experts and stakeholders, including government agencies, regulatory authorities, farmers' organizations and academics to formulate a coordinated plan to guide the orderly phasing out of antibiotics for non-therapeutic uses in animal production in Zambia.

This report outlines the five-year roadmap as devised and agreed by all stakeholders. It is therefore expected that all players will judiciously execute their role to protect the ever-shrinking arsenal of antibiotics as our shared resource for the furtherance of humankind.

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Foreword

Antibiotic misuse and overuse in food-animals such as chicken, cattle and fish is one of the major reasons for growing antimicrobial resistance (AMR). AMR—antibiotic resistance in particular—is not only a huge public health crisis, but will also heavily impact food security and safety, livelihood and development, specifically in low- and middle-income countries.

But this is where there is an opportunity—and it concerns how we build our food system. Today, a substantial portion of antibiotics produced globally are used in food-animals—primarily for non-therapeutic uses such as growth promotion and disease prevention. This has to do with the industrial system of food production, which then requires governments to invest heavily in mitigating the harmful effects of toxins in the environment and in human health. Efforts to phase out non-therapeutic use of antibiotics will yield huge benefits in containing AMR. This explains the ongoing global push to eliminate use of antibiotics as growth promoters, and many countries, including a few low- and middle-income countries, have already claimed to having stopped such misuse.

A bigger challenge is to reduce preventative mass medication, which involves indiscriminate antibiotic use in groups of healthy animals and is an easy and cheap substitute for good husbandry practices in high-density intensive farm systems. This practice is steeply growing in developing parts of the world to meet the demand for animal protein. Another significant concern has been the animal use of antibiotics that are of critical importance to humans. The increased use of these life-saving antibiotics in animals makes them less effective for humans. Discontinuing their use in animals will best preserve them for humans. Work towards this has begun globally—one of the targets set is to immediately stop animal use of highest priority critically important antibiotics (HPCIAs), including polymyxins such as colistin, quinolones, third- and fourth-generation cephalosporins, macrolides and glycopeptides.

This report presents a five-year roadmap to phase out non-therapeutic antibiotic use and critically important antibiotics in the poultry and cattle sectors in Zambia. It shows how an emerging country like Zambia is getting itself ready to systematically address the One Health challenge. The report is developed in consultation with experts and stakeholders of the national Antimicrobial Resistance Coordinating Committee such as the Zambia National Public Health Institute, Ministry of Fisheries and Livestock and Zambia Medicines Regulatory Authority. We hope that the government of Zambia formulates the necessary policies and programmes to support this plan.

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Abbreviations

AGP—Antibiotic Growth Promoter
AMR—Antimicrobial Resistance
AMRCC—Antimicrobial Resistance Coordinating Committee
CIA—Critically Important Antimicrobial
CSE—Centre for Science and Environment
DAZ—Dairy Association of Zambia
DVS—Department of Veterinary Services
ESBL—Extended Spectrum Beta Lactamase
FAO—Food and Agriculture Organization of the United Nations
GDP—Gross Domestic Product
HPCIA—Highest Priority Critically Important Antimicrobial
IACG—Interagency Coordination Group
LMIC—Low- and Middle-Income Country
MFL—Ministry of Fisheries and Livestock
MT—Metric Tonne
NAP—National Action Plan
OIE—World Organisation for Animal Health
SI—Statutory Instrument
UNZA—University of Zambia
VAZ—Veterinary Association of Zambia
WHO—World Health Organization
ZAMRA—Zambia Medicines Regulatory Authority
ZNPHI—Zambia National Public Health Institute

1. Introduction

Antimicrobial resistance (AMR), particularly antibiotic resistance, is a global public-health threat. The misuse of antimicrobials in humans and animals is considered a driver of AMR. A substantial portion of overall antibiotic use is said to be in food-producing animals, where it is used for therapeutic and non-therapeutic purposes. Therapeutic use refers to use of antibiotics for the treatment of an animal with a clinically diagnosed infectious disease or illness.[1] Non-therapeutic use involves (a) use of antibiotics to increase the rate of weight gain and/or the efficiency of feed utilization in animals (growth promotion), or (b) their use in healthy animals to prevent any risk of infection or control the larger dissemination of a clinically diagnosed infectious disease identified within a group of animals (disease prevention).[2] In reality, there could be an overlap, i.e., an antibiotic given for growth promotion could prevent disease or vice-versa. The routine exposure of antibiotics to animals in sub-optimal doses is one of the factors that leads to the emergence, selection and dissemination of resistant bacteria, thereby adding to the burden of AMR. Of the commonly used antibiotics in food-animal production, many are regarded critically important for human medicine.

Globally, there has been growing momentum to limit antibiotic misuse in food-animal production. AMR Action Plans from the World Health Organization (WHO) as well as the Food and Agriculture Organization of the United Nations (FAO) highlights the need for necessary policies to phase-out antibiotic growth promoters in animals.[3,4] The WHO guidelines on use of medically important antimicrobials in food-animals recommend complete restriction on use of all classes of medically important antimicrobials for growth promotion and disease prevention.[5] The guidelines further recommend not using highest priority critically important antimicrobials (HPCIAs)[6] as therapeutic agents in food-animals. The Interagency Coordination Group (IACG) on AMR in 2019 reinforced the need for an urgent action to phase out the use of antimicrobials for growth promotion starting with an immediate end to the use of HPCIAs.[7] It also highlighted the need for collateral measures to address challenges arising from the phase-out of antimicrobials, such as improved hygiene, sanitary and biosecurity measures; use of vaccines, probiotics, phytochemicals; and economic incentives to farmers. The World Organisation for Animal Health (OIE) also recognized the need for phasing out the use of antimicrobials for human health as growth promoters in animals, and adopted a revised list of antimicrobial agents of veterinary importance in 2018.[8,9] The list recommends that the responsible and prudent use of antimicrobial agents does not include the use of antimicrobial agents for growth promotion in the absence of risk analysis. WHO-categorized HPCIAs are also highlighted to be the highest priorities for countries in phasing out use of antimicrobial agents as growth promoters. The OIE list further recommends that the use of colistin along with antibiotics under classes fluoroquinolones and third- and fourth-generations of cephalosporins as growth promoters should be urgently prohibited. These should also not be used for preventive treatment in the absence of clinical sign of a disease in an animal, or as a first line treatment unless justified. Their use as a second-line treatment should ideally be based on bacteriological test results.

Countries across the globe have also begun efforts to contain antimicrobial misuse in animals. As of 2017, 110 countries have claimed to have stopped use of antibiotic growth promoters (AGPs) in food-animals.[10] Further, 64 countries have reported limiting the use of critically important antimicrobials (CIAs) for growth promotion in animal production.[11] Many countries have also come up with similar initiatives

after that. For example, the use of colistin in food-producing animals was banned in India in 2019. The phase-out of non-therapeutic use of antimicrobials is however expected to be a greater challenge in many low- and middle-income countries (LMICs) owing to a high burden of infections, inadequate sanitation practices, poor waste management, limited availability of diagnostic facilities and the general under-investment in veterinary services to promote animal health.

The non-therapeutic use of antibiotics for prophylaxis (disease prevention) and growth promotion in food-animal production is a known issue in Zambia, across different sectors. Emerging resistance in bacteria isolated from food-animals has been reported in different studies in the country. The Zambia's National Action Plan (NAP) on AMR[12] emphasizes on optimized antimicrobial use, regulation of antimicrobial availability, and stewardship programmes in animal health. A number of efforts to strengthen the regulatory framework on the use of antimicrobials and to combat the emergence and spread of AMR in Zambia are being undertaken. The notable ones include the ongoing review of different pieces of legislation on AMR and antimicrobial use, and drafting of regulations on Animal Feed and Slaughter facilities. In view of this, it was recognized that there is a need for consultation and consolidation of a way forward regarding the phasing out of non-therapeutic use keeping in mind the ground realities of the country.

As part of the existing collaboration to support the implementation of Zambia's multi-sectoral NAP on AMR, the Zambia National Public Health Institute (ZNPHI) and the Centre for Science and Environment (CSE) jointly organized a two-day workshop in August 2019 that focused on development of a roadmap to phase-out non-therapeutic use of antibiotics and use of CIAs in poultry and cattle being the two main animal species produced in the country. The Zambia Medicines Regulatory Authority (ZAMRA) is working on a draft Statutory Instrument (SI) to regulate the usage of antimicrobials in animals. The deliberations in the workshop took place in this backdrop. Under the guidance of the Antimicrobial Resistance Coordinating Committee (AMRCC) this was achieved with the help of technical experts from Ministry of Fisheries and Livestock (MFL), ZAMRA, Veterinary Association of Zambia (VAZ), Dairy Association of Zambia (DAZ), Livestock Services Cooperative Society, University of Zambia (UNZA), the feed industry and the human-health sector. This report is an outcome of this workshop. It is a proposed way forward which will be considered by the Government of Republic of Zambia.

2. Overview—Food-animal sector in Zambia

The Department of Veterinary Services (DVS), under the MFL, is responsible for animal-health services. It works with other departments, agencies and the private sector towards providing these services. The food-animal sector in Zambia comprises animals such as cattle, poultry, pigs, goats, sheep and fishes. Livestock makes up 42 per cent of the total agricultural contribution to the total GDP of the country.[13] Animal products contribute to about 23 per cent of the per capita supply of protein in Zambia.[14] The major sources of animal protein are beef, chicken, pork, fish, milk and eggs.

With a rapidly growing human population, the demand for animal protein is on the rise. However, the sector has experienced low production owing to a range of factors including high disease prevalence and poor animal husbandry.[15] Increase in intensive farming systems is associated with increase in the use of antimicrobials and vitamins and other supplements to enhance growth. All antibiotics used in the veterinary sector in Zambia are imported as the country has no manufacturing firms for veterinary pharmaceuticals. Around 11 metric tonnes (MT) of antibiotics were imported for veterinary use in 2017, of which the major classes included tetracyclines, sulfonamides, fluoroquinolones, and penicillins.[16] Antibiotic use for disease prevention is not prohibited in Zambia, with the most prevalent practice being the use of anticoccidiostats in feed formulations. While there is no specific legislation against the use of antibiotic use for growth promotion, it is generally discouraged and it is recognized that this practice is done by some players in the sector.

To contain antibiotic misuse in animals, ZAMRA is currently working on a draft statutory instrument (SI), which outlines the regulations for use of antimicrobials in animals. The proposed legislation aims to debar the registration, distribution or marketing of AGPs through feed (as additives or premixes), drinking water or any other means on a routine basis. It also prohibits compounding of antimicrobials with feed, feed premixes, feed additives, vitamins or herbal preparations. The proposed SI will further prohibit the use of three classes of CIAs in animals, namely fluoroquinolones, third- and fourth-generation cephalosporins, polymyxins, along with phenicols.

2.1 Poultry

The poultry sector in Zambia, largely comprising indigenous, layer and broiler chickens, has seen tremendous growth in recent years. The total broiler population in Zambia was 6.76 million, with Lusaka, Copperbelt and Central provinces producing nearly 75 per cent of the total broiler birds in Zambia, as of 2018.[17] The total layer population was 1.67 million, with Lusaka, Central and Copperbelt provinces being the key layer poultry-producing provinces in the country.[18] Chicken meat production in 2018 was 5.11 million MT and the total number of eggs produced were 1.64 million.[19]

Antibiotic use in the Zambian poultry sector is prevalent. Some of the commonly used antibiotics include gentamicin, neomycin, doxycycline, tetracycline, enrofloxacin, tylosin, amoxicillin, sulfadimidine sodium, sulfadiazine, colistin, chloramphenicol and ceftiofur. Zinc bacitracin is the only registered antibiotic with an indication for growth promotion. However, antibiotics such as avilamycin, flavomycin, olaquindox and virginiamycin have been used for growth promotion in the poultry sector. Varying levels of resistance against some antibiotics has been reported in some scholarly studies done in the country. For instance, ESBL *E. coli* isolated from chicken displayed a wide range of resistance (20.8–100 per cent) to multiple antibiotics, including CIAs

such as ampicillin, ciprofloxacin, streptomycin etc.[20] In another study, *Salmonella* spp. isolated from commercially processed broiler carcasses was found to be resistant to gentamicin and tetracycline antibiotics.[21] Most of these studies were limited in that they focused on one species, with limited geographic coverage. There is need for countrywide surveillance to be undertaken to differently ascertain the resistance patterns observed in some of these studies.

2.2 Cattle

Cattle are raised in Zambia both for meat and milk. The total cattle population in 2018 was 3.71 million.[22] The Southern province in Zambia accounted for the highest number of cattle, at 35.4 per cent, followed by Central province at 22.5 per cent.[23] At 43.2 per cent, cows accounted for the largest category of cattle raised.[24] In 2018, around 6.10 million MT of beef and 1.68 million MT of milk (from all milk-producing animals) were produced in the country.[25] Antibiotics are used in the cattle sector, with some of the commonly used being penicillin, streptomycin, enrofloxacin, amoxicillin, sulfadimidine sodium, tetracycline, doxycycline and oxytetracycline. There is no information as to whether AGPs are used in the cattle sector in Zambia, but antibiotics are used for prophylactic or therapeutic purposes. Antibiotic resistance has also been reported in cattle in studies that were conducted across few provinces in Zambia. In all these studies, *E. coli* isolated from beef, dairy and pastoral cattle samples have been found to exhibit varying range of resistance (1.2–96.4 per cent) to multiple antibiotics including CIAs such as ampicillin, kanamycin, streptomycin.[26–29] High resistance against multiple antibiotics such as amoxicillin, ampicillin, co-trimoxazole, erythromycin, gentamicin and penicillin has also been found in *Enterococci* sp. isolated from pastoral cattle.[30]

2.3 Pig

The total pig population in the country was 1.08 million in 2018 of which Eastern province accounted for the highest percentage, at 28.3 per cent, followed by Southern province at 16.8 per cent.[31] The number of households raising pigs was 0.17 million in the same year, with Lusaka and Copperbelt provinces having the highest proportion of households.[32] The number of establishments raising pigs were 263.[33] The average number of pigs per household and establishment were 5.8 and 181 respectively.[34] Pork production in 2018 was 0.56 million MT. Major antibiotics used in pigs are streptomycin, tetracycline, enrofloxacin, tylosin, amoxicillin, penicillin, sulfadimidine and sulfathiazole.

2.4 Fish

Even though Zambia is a landlocked country, fisheries form an important sector. Fish in Zambia is largely captured from rivers or lakes. Fish farming or culture-based fisheries (aquaculture) are steadily growing. A total of 9,615 households and 126 establishments were involved in fish farming countrywide in 2018.[35] Northern province had the highest proportion of fish-producing households (33.9 per cent) and establishments (19.8 per cent) in the country.[36] In 2017, a total of 21,567.1 MT of fish were produced, of which establishments contributed 15,997 MT (74 per cent) while households contributed 5,570 MT (26 per cent).[37] The highest production from households was recorded in Northern province (38 per cent), Luapala (15.1 per cent), and Lusaka (11.5 per cent) and that from establishments was recorded in Southern province (76.1 per cent) followed by Lusaka (8.4 per cent) and Northern province (7.3 per cent).[38] There have been no reports of antibiotic use in fish farming in Zambia.

3. Roadmap to phase out non-therapeutic antibiotic use and critically important antibiotics in food-animals in Zambia

3.1 Approach

A five-year roadmap, starting 2020, was developed in order to guide the phase-out of non-therapeutic antibiotic use and CIAs in the poultry and cattle sectors. These sectors were selected over the pig and fish sectors based on their importance and antibiotic use trends. Across these sectors, the roadmap was discussed under the following broad themes:

- Antibiotic use of growth promoters through feed
- Routine antibiotic use for disease prevention (prophylactic use)
- Use in animals of antibiotics considered critically important in humans

The roadmap follows a two-phased approach. The time required to phase out antibiotics is classified into one year, and two to five years. Experts also identified relevant government policies and programmes that should be initiated, chemical or non-chemical alternatives, biosecurity measures and good animal husbandry practices to support the phase-out plan. Experts proposed that a roadmap for prohibiting antibiotic misuse in the pig and fish sectors is also subsequently developed.

3.2 Roadmap—Poultry and cattle sector

The roadmap to phase out antibiotic use in food-animal sector in Zambia is shown in *Table 1: Roadmap to phase out non-therapeutic antibiotic use and critically important antibiotics in poultry and cattle sectors in Zambia.*

Table1: Roadmap to phase out non-therapeutic antibiotic use and critically important antibiotics in poultry and cattle sectors in Zambia

	One year	Two to five years
BROILER AND LAYER POULTRY		
Growth promotion	• Third- and fourth-generation cephalosporins • Quinolones (e.g. enrofloxacin, ciprofloxacin) • Polymyxins (e.g. colistin) • Tetracyclines (e.g. oxytetracycline, doxycycline) • Phenicols	Virginiamycin Zinc bacitracin Flavomycin Olaquindox Avilamycin Remaining AGPs
Prophylaxis (Disease prevention)	All CIAs, for example • Third-, fourth- and fifth-generation cephalosporins • Glycopeptides • Macrolides and ketolides (e.g. tylosin) • Quinolones (e.g. enrofloxacin) • Polymyxins (e.g. colistin) • Aminoglycosides (e.g. gentamicin, neomycin) • Penicillins (e.g. amoxicillin)	All prophylactic antibiotics that are packaged along with vitamins
Therapeutic use	• Colistin (phase-out) • Enrofloxacin for broilers and layers (restricted use)* • Tylosin for layers (restricted use)	
CATTLE FOR MILK AND MEAT**		
Therapeutic use	• Colistin (phase-out) All other HPCIAs (restricted use): • Third-, fourth- and fifth-generation cephalosporins • Glycopeptides • Macrolides and ketolides (e.g. tylosin) • Quinolones (e.g. enrofloxacin) • Polymyxins (other than colistin)	

*Restricted use of antibiotics could include its use only under prescription guided by antimicrobial susceptibility testing and not using it as a first-line drug.

**Antibiotics are not commonly used for prophylaxis in cattle except for mastitis. Oxytetracycline, which is used metaphylactically in addressing tick-borne disease outbreaks, could be considered for phase-out in the future.

The phase-out should be accompanied by the gradual use of alternatives and better farm-management practices. Chemical alternatives such as organic acids, disinfectants, water sanitizers; and non-chemical alternatives such as vaccines, probiotics, prebiotics, in-feed enzymes, herbal products, essential oils and antioxidants should be considered for use to prevent chances of infection leading to unnecessary antibiotic use. Use of better disinfection practices and prevention of animal overcrowding at farms should be considered to prevent occurrence and spread of infections. Better biosecurity and animal husbandry practices like isolation of sick birds and/or animals, use of footbaths, and proper disposal of carcasses should be ensured in parallel.

The process of phase-out should also be supported by various government-based policies and programmes, including programmes to:

- Sensitize and engage relevant stakeholders such as drug inspectors, veterinary professionals and para-veterinary professionals, extension officers, farmers, drug dealers and agrovet dealers to create awareness about responsible antibiotic use in animals and better farming practices.
- Incentivize farmers for better farming practices and farm biosecurity.
- Encourage research and availability of chemical and non-chemical alternatives such as prebiotics, probiotics etc.
- Involve the alternative industry for supporting the public-health initiative.
- Monitor AMR and antibiotic residues in the food-animal sector.
- Develop biosecurity and sanitation guidelines for farm establishments.
- Develop national therapeutic guidelines to outline treatment use of antimicrobials in animals.
- Ensure early disease reporting in farm animals.
- Ensure up-to-date vaccination of farm animals.
- Ensure development of dipping programmes for control of tick borne diseases.
- Conduct national wide AMR surveillance in animals to determine level of risk and inform further action on restriction of use of antimicrobials.

Factors to be considered during phase-out:

- Therapeutic use of CIAs should be allowed only under veterinary supervision and prescription.
- Antibiotics that can replace the banned or restricted CIAs should be determined based on culture and sensitivity tests.
- The government should, in parallel, develop necessary policies for monitoring of agrovet shops in Zambia from which these drugs are generally procured.
- Alternatives to antibiotics should be made available, and handled only by professionals.
- Research to discover more alternatives should be encouraged and continued.
- Feed and feed additives should be tested for banned antibiotics.
- Over time, the quantities of antibiotics used and imported should decrease.
- Removal of antibiotics should produce no economic impact.
- All the regulations that promote the rational use of antimicrobials should be finalized and implemented.

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Notes:

This report presents a roadmap to phase out non-therapeutic use of antibiotics and critically important antibiotics in food-animals in Zambia. The report is an outcome of a workshop organized jointly by the national Antimicrobial Resistance Coordinating Committee through the Zambia National Public Health Institute and the Centre for Science and Environment, India.

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