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3-Year System Business Plan Companion Document

Action 1 - CGIAR Contributions to Mitigating Agriculture-Associated Antimicrobial Resistance in Low- and Middle-Income Countries

Prepared by:	A4NH in consultation with Centers/Science Leaders
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1. This document summarizes CGIAR's interests and plans in contributing to mitigating antimicrobial resistance (AMR) associated with agriculture, including livestock, aquaculture, and crop production, in low and middle-income countries, and its implications for public health globally.

Introduction

2. Antimicrobials are among the most important tools available to medical and veterinary professionals for curing disease and improving welfare, however, they are threatened by the emergence of AMR. The resulting lack of treatment options for infectious diseases in people and livestock jeopardizes human health as well as animal health, food and nutrition security, and livelihoods. The World Bank estimates that increasing drug resistance could reduce global livestock production by 7.5 percent. The main driver of AMR emergence is the selection of resistant bacteria following use of antibacterial compounds. Misuse is of growing concern and engenders negative consequences without health benefits. AMR of human-specific pathogens is largely due to medical use, however, agriculture has also been linked to AMR emergence. Depending on compounds used, humans, livestock, and fish excrete unmetabolized drugs, leading to contamination of the environment, including water systems, and adding to the complexity of AMR. This is a concern in intensifying livestock production and aquaculture systems that have direct linkages to water systems important for food production and water consumption. The complexities around AMR call for interdisciplinary solutions, bringing together social and biosciences from public health, veterinary, and environmental sectors.

3. **Livestock**

a. **In low and middle-income countries**, little is known about antimicrobial use in agriculture or how close interactions of livestock and people in smallholder production systems and emerging intensive production systems relate to AMR emergence. Counterfeit drugs, lack of regulations, and poor observance of withdrawal periods resulting in antimicrobial residues in animal-source foods pose challenges, coupled with limited incentives and lack of cost-effective, viable alternatives for reducing antimicrobial use. Poor knowledge amongst actors involved, from livestock keepers and producers to even some veterinary professionals and government officials, compounds the problem and highlights the need for capacity building at all levels. The lack of capacity is also apparent in surveillance systems, which require reliable and credible laboratories to detect new resistance patterns and process many samples to monitor AMR in livestock, livestock products, human populations, and to support monitoring and compliance systems to enforce regulations. Understanding livestock-associated AMR's contribution to disease-resistant infections in humans requires novel, interdisciplinary collaboration between One Health (veterinary, environmental and public health) researchers, and the development of common tools and integrated research procedures.

b. **In many high-income countries**, stringent regulations on antimicrobial use in livestock agriculture coupled with incentive systems have been put in place, and the careful monitoring of antibiotic consumption is increasing as a result. These countries demonstrate that with good husbandry and herd health practices, antibiotic use can be reduced without any undue effects on productivity. These experiences provide lessons that can be adapted by others, particularly in emerging middle-income countries.

4. **Aquaculture**

a. **Aquaculture is an important and growing industry globally, with low and middle-income countries being well integrated in the global seafood trade**. Projections suggest that aquaculture production will double by 2030 worldwide. Aquaculture systems are complex and dynamic, with many factors driving the (mis)use of antimicrobials. Use in aquaculture is different to that in humans and livestock species, since antimicrobials are administered directly into the aquatic environment, usually through medicated feed, increasing the potential for contamination and spread. Unlike terrestrial farming, in aquaculture, antimicrobials and feed are often supplied separately to farmers, in many parts of the world without involvement of an authorized veterinarian. Farmers then must mix the antimicrobials with the feed, resulting in a high potential risk of occupational exposure. Moreover, fish do not metabolize antimicrobials effectively, and it has been estimated that 75 percent of antimicrobials fed to fish will be excreted back in their active form into the aquatic environment.

b. **In low and middle-income countries**, antimicrobials are used extensively in aquaculture as "cure-all" and "increase productivity" strategies, to compensate for weaknesses in management and hygiene and lack of alternate fish health tools such as diagnostics and vaccines. Regulation for the responsible use of antimicrobials is often inefficient and surveillance or monitoring in many countries is lacking or absent. Efficient surveillance is in place in many production systems targeting export markets, but often absent in fish supply chains for domestic markets. Regulatory approaches with effective enforcement can lead to substantial reduction in antimicrobial use, as well as appropriate use of commercial vaccines for some fish species, as demonstrated in some high-income countries. As with livestock, high production and fish health standards have demonstrated that it is possible to achieve high productivity levels without antimicrobials.

5. **Crops**

a. **Plant diseases place substantial constraints on agricultural production in low and middle-income countries.** Antimicrobial use to control plant diseases is presently very limited but may increase rapidly in response to the emergence and spread of epidemic diseases, such as citrus greening disease.

CGIAR's current endeavors on AMR risk mitigation

6. With its mandate to improve livelihoods of poor people through agriculture and food research, CGIAR is ideally positioned to tackle agriculture-related AMR risks in low and middle-income countries and to test and promote solutions to mitigate risks.

7. As a result, the CGIAR research portfolio's focus on AMR has steadily grown in recent years in two CGIAR Research Programs (CRP Livestock, led by the International Livestock Research Institute (ILRI) and Agriculture for Nutrition and Health (A4NH), led by the International Food Policy Research Institute (IFPRI)) and links to a third CRP on Fish, led by the World Fish Center.

8. This portfolio of projects includes grants focusing on antimicrobial use and on AMR emergence in risk hot spots characterized through close interactions of people, animals, and environment (One Health):

a. **CRP Livestock and A4NH** contribute to research on the complex pathways of AMR. Both programs start with the use of antimicrobials in livestock and fish production, with CRP Livestock focusing on the livestock health impacts and A4NH on the implications for human health.

b. **CRP Livestock** concentrates on antimicrobial use and productivity since AMR will lead to treatment failure in livestock. It aims to promote rational and efficient use of antimicrobials and, more explicitly, how rational use can be promoted when integrated into herd health packages. This will be achieved through

building capacity, testing alternatives to antimicrobials, and creating incentives to refine their use. Outputs of the different studies provide evidence and convincing arguments to engage policymakers in the AMR discussion, and CRP Livestock aims to support countries in setting up appropriate antibiotic use strategies for livestock.

c. **A4NH** focusses on understanding the drivers of AMR emergence in livestock and fish systems and their implications for human health. To better understand human AMR risks due to antimicrobial use in agriculture, studies into the biology, ecology, and epidemiology of microbes across livestock and fish production, environment, and public health contexts are conducted in specific sites. Whole genome sequencing helps identifying movement of AMR genes between these areas and drivers of AMR emergence and transmission. To test how these drivers can be mitigated, intervention studies will be conducted in hotspot sites. Evidence from these studies will then be used to support informed policy decisions in relevant sectors.

ILRI as host of the CGIAR AMR Hub

9. ILRI leads the AMR components of both CRP Livestock and A4NH. Through ongoing research, ILRI has established strong partnerships with other key players in AMR research, including the Swedish Agricultural University (SLU), London School of Hygiene and Tropical Medicine (LSHTM), University of Liverpool and the Royal Veterinary College, and works on international One Health and livestock sector platforms with WHO, OIE, FAO, and the African Union. Significantly, through LSHTM's role as a managing partner in A4NH, public health research partnerships have been strengthened, creating capacity to design and evaluate interventions that demonstrably reduce the risk of disease-resistant infections in humans arising from agriculture.

10. Being a CGIAR center, ILRI has close links to other centers and CRPs beyond Livestock and A4NH. ILRI has its headquarters in Nairobi, Kenya, a principal campus in Addis Ababa, Ethiopia, and 14 country offices throughout Africa and Asia with ongoing research projects in many more countries. ILRI hosts six other CGIAR centers in Nairobi and 11 in Addis Ababa. As with other CGIAR centers, over the years, ILRI has established close collaborations with national agricultural research systems and, more recently, with public health research institutions through A4NH. This provides a very strong network of national partners on the ground.

11. In addition to these relationships, ILRI also hosts, on behalf of the African Union/NEPAD, the Bioscience east and central Africa-ILRI (BecA-ILRI) Hub, a shared agricultural research and biosciences platform to increase access to affordable, world-class research facilities. The BecA-ILRI Hub provides a shared biosciences research platform, research-related services, and capacity building opportunities to eastern and central Africa and beyond.

AMR-Hub strategy

12. To tackle AMR challenges in low and middle-income countries and ensure the sustainability of global food and health systems, **we propose embedding a CGIAR AMR-Hub at ILRI with global AMR research and development efforts such as the proposed interdisciplinary Centre of Excellence in Denmark** (further details to follow).

13. This approach will help foster learning from past experiences, support AMR research excellence in the global south, and ensure a critical mass of research to find suitable and sustainable solutions. ILRI will be responsible, through its co-leadership of A4NH One Health and AMR research, for bringing in other important CGIAR and partner capacity. LSHTM, as co-lead with ILRI in this work under A4NH, provides an ongoing and credible public health partnership that can be built upon in the proposed Center-Hub model. Also, importantly, ILRI will work closely with IFPRI, A4NH's lead center, to leverage IFPRI's in-country policy support activities to link AMR policy and regulation discussions into the broader food and development policy arena in multiple low and middle-income countries and globally.

14. **The CGIAR AMR strategy builds on five pillars of research and interventions**:

    a. Understand knowledge, attitude, practices, and incentives for antimicrobial use or reduction in use and role of formal and informal markets. This includes distribution networks, types of products used, and the way in which new antimicrobials, particularly those classified by WHO as Critical Important Antibiotics (CIA), are used;

    b. Research AMR transmission dynamics at the human-animal-environmental interface in different agricultural systems;

    c. Design and evaluate interventions to reduce and more effectively use antimicrobials in agriculture in low and middle-income countries;

    d. Support evidence-based policy dialogue for antimicrobial surveillance and AMR strategies; and

    e. Capacity development.

15. **Geographical reach**: the AMR-Hub aims to support the efforts of low and middle-income countries globally, drawing on the lessons from high-income countries, particularly Denmark and others in Europe. The current research partnership around ILRI has a strong presence in Africa and Asia, with links in South America under development.

16. Below is an overview of proposed activities under each of the five pillars to be coordinated through the AMR-Hub:

    a. <u>Understand knowledge, attitude, practices, and incentives for antimicrobial use in low- and middle-income countries and role of formal and informal markets:</u>

        i. Collect and collate data on use of antimicrobials in livestock, aquaculture, and crops (antibiotic classes, dosage);

ii. Understand stakeholder behavior for antimicrobial use;
iii. Assess quality and governance of antimicrobials used in humans, livestock, fish, and crops;
iv. Understand incentives and rationales for antimicrobial use in agricultural systems; and
v. Conduct research on formal and informal antimicrobial markets and access of producers to these markets.

b. Research AMR transmission dynamics at the human-animal-environmental interface in different agricultural systems:
   i. Collect data on the extent of antimicrobial-resistant bacteria found in livestock, fish, humans, the environment, and food;
   ii. Conduct research to understand the transmission and genetic mechanisms of resistance in agriculture and the implications for human and animal health; and
   iii. Develop a range of mathematical and biological models of AMR in low- and middle-income countries to understand the relative contribution of agricuturally-associated AMR to the human AMR burden and risk of drug resistant infections in different contexts.

c. Design and evaluate interventions and incentives to reduce antimicrobial use in agriculture in low- and middle-income countries:
   i. Develop and evaluate the impact of a range of local interventions in agricultural systems to reduce AMR risks to human populations, taking a transdisciplinary approach which engages researchers and stakeholders from different sectors;
   ii. Develop and test gender-sensitive pest and pathogen controls to better manage livestock and fish diseases and reduce the use of antimicrobials;
   iii. Explore feasibility of incentive-based systems, especially intensifying production systems;
   iv. Understand the costs and benefits of interventions to tackle AMR, at different levels of analysis (stakeholder, value chain, national);
   v. Characterise gender-differential impacts of interventions on poor farmers, vulnerable groups and address other societal objectives such at attaining nutrition security; and
   vi. Understand the potential of market demand/pull for responsibly-produced foods (animal source foods, fish, and crops).

d. Support evidence-based policy dialogue for antimicrobial surveillance and AMR strategies:
   i. Synthesize evidence on antimicrobial use and AMR to influence public policy and the development of credible, enforceable regulations and other interventions that reduce antimicrobial use;
   ii. Generate evidence to promote good practices in the governance, supply, use, and disposal of agriculture-associated antimicrobials and identify incentives that facilitate their adoption;

iii. Engage policymakers in agriculture and health, and encourage integrated policy approaches supported by experimental evidence, in the context of One Health solutions;
iv. Pilot and evaluate approaches for surveillance of use of antimicrobials, treatment failure, and AMR; and
v. Contribute to mapping existing and projecting future use of antimicrobials in the face of increasing intensification.

e. Capacity development:
   i. Support capacity building and increase awareness of AMR in the agricultural sector (veterinarians, livestock and fish producers, and service providers);
   ii. Support exchange programs for LMIC researchers with the AMR Centre of Excellence in Denmark and other affiliated institutions;
   iii. Provide and facilitate access to research facilities for researchers from low and middle-income countries; and
   iv. Organize and run training programs on AMR, including research and mitigation, using modern online and interactive formats as appropriate to the intended audience