



Muscat Ministerial Manifesto on Antimicrobial Resistance

Statement by Antibiotic Resistance Coalition members*

November 2022

We are pleased to see that the Third Global High-Level Ministerial Conference on Antimicrobial Resistance (November 24-25, 2022) will once again lift up this important global, intersectoral challenge to the attention of governments. While few from the ranks of civil society will be in attendance, we have noted the potential importance of the [Muscat Ministerial Manifesto on Antimicrobial Resistance](#) (AMR). Like those who might sign this Manifesto, we too are pleased to see the UN Environment Program being welcomed into the Quadripartite and hope this will strengthen actions to take into account the environmental dimensions of a One Health response to AMR.

The Manifesto states that in 2019, the United Nations Secretary-General had “called upon Member States to deliver the urgent support and investment needed to scale up AMR responses at national, regional, and global

levels,” but recognizing again that “there are inadequate financial resources available for the sustainable implementation of national action plans on AMR and to support research and development of innovations” beckons for further explanation. We are pleased to see the recent return in 2022 of a [survey item in the Tracking Antimicrobial Resistance Country Self-Assessment Survey \(TrACSS\)](#) that captures financial provision for the National AMR action plan (item 2.3) after its removal in the 2021 survey year results. Such tracking is critical to ensure that rhetoric is matched by resources. Still four years after the UN Secretary-General has called for greater resourcing, we must ask how it is possible that fewer than a third of countries reporting in TrACSS (28%) can say that they have “costed and budgeted operational plan[s]” or included “financial provision for the National AMR action plan implementation” in their national plans and budgets. Similarly, what

*** Members of the Antibiotic Resistance Coalition signing in support of this joint statement include:**

- Alliance to Save our Antibiotics
- Consumers Association of Penang
- European Public Health Alliance (EPHA)
- Food Animal Concerns Trust (FACT)
- Health Action International
- Health Care Without Harm
- Pan-African Treatment Access Movement (PATAM)
- ReAct Africa
- ReAct Asia Pacific
- ReAct Europe
- ReAct Latin America
- ReAct Strategic Policy Program
- Sahabat Alam Malaysia (Friends of the Earth Malaysia)
- Society for International Development
- Third World Network
- Universities Allied for Essential Medicines (UAEM)

could explain that the level of commitments received globally by the [Antimicrobial Resistance Multi-Partner Trust Fund total just over US\\$26 million](#) after having seen the trillion-dollar price tag of lack of preparedness in tackling emerging infectious diseases such as the COVID-19 pandemic?

The Manifesto does briefly allude to “the impacts of the COVID-19 pandemic on our efforts to respond to AMR, while also noting that the pandemic has demonstrated critical links between humans, animals and the environmental ecosystem, underlining our shared responsibility to prevent, prepare for, and respond to emerging and re-emerging AMR threats through sustainable investments and actions that strengthen human and animal health systems.” However, in the call to action that follows, the opportunity of finding synergy between investing in AMR and in pandemic preparedness and response is missing. While none of the Oman Ministerial sessions on the proposed agenda explicitly tackles the connection between AMR and the pandemic, the parallel session topics could provide strategic foundation for supporting investments that build on such synergy—efforts to tackle zoonotic disease transmission, [integrated disease surveillance such as a global wastewater surveillance network](#), infection prevention and control, and surge capacity for delivering health commodities. We hope that this connection is not missed as formal negotiations begin over the “zero draft” of a pandemic instrument at the Intergovernmental Negotiating Body’s meeting from December 5-7, 2022.

A potentially significant advance in the Muscat Ministerial Manifesto on AMR is the announced commitment to three targets:

- **Target 1:** Reducing the total amount of antimicrobials used in the agri-food system by at least 30-50% from the current level by 2030;
- **Target 2:** Zero use of medically important antimicrobials for human medicine in animals for non-veterinary medical purposes or in crop production and agri-food systems for non-phytosanitary purposes; and
- **Target 3:** Ensuring that ACCESS group antibiotics comprise at least 60% of overall antibiotic consumption in humans by 2030.

We welcome the efforts to begin setting targets, by country context and in the healthcare delivery and food production sectors. Targets to reduce use of antimicrobials are important but must rely upon effective and credible governance and accountability. The setting of targets must consider local context, and countries require resources to enable them to follow through on implementing targets.

Target 1: Reducing the total amount of antimicrobials used in the agri-food system by at least 30-50% from the current level by 2030

The range of “at least 30-50% by 2030 from the current level” affords latitude based on context. As discussed in the Appendix to the Manifesto, such flexibility accounts for differences in country context and resource availability. Some countries have made significant strides in lowering levels of antimicrobial use in food production, but also may have started from higher baselines of such use. The examples given, from the Netherlands (50% in 5 years) to China (57% in 5 years), offer some assurance of the feasibility of implementing such targets, at least in high- and middle-income countries where such antimicrobial use in food production disproportionately also occurs. However, the Manifesto language, as opposed to the Appendix, might provide stronger guidance to deter high-end country users of antimicrobials from just doing the minimum, regardless of whether they could or should do more. Compliance with the targets depends on reliable and agreed upon baselines. At the same time, the disparate impact on small-scale producers as opposed to large-scale farming operations from implementing such targets must also be considered, and fair and equitable plans must be put in place and resourced to transition smallholder farmers.

However, such accountability requires transparency of antimicrobial use and antimicrobial resistance data, at least at the country level. [One out of four countries \(40 out of 157; 26%\) still report use of antimicrobials as growth promoters](#), but the World Organization for Animal Health still keeps the identity of these countries anonymous and non-transparent in its annual surveys. In 2017, the [top ten consumers of veterinary antimicrobials](#) were China (45%), Brazil (7.9%) and the United States (7.0%), followed by Thailand (4.2%), India (2.2%),

Iran (1.9%), Spain (1.9%), Russia (1.8%), Mexico (1.7%), and Argentina (1.5%). Three of these countries—all upper middle-income or high-income—comprise nearly 60% of the global consumption of veterinary antimicrobials. We will be watching to see whether those countries most responsible for the disproportionate share of antimicrobial use globally in food production step forward to make these commitments or whether those with much less to contribute sign instead.

Target 2: Zero use of medically important antimicrobials for human medicine in animals for non-veterinary medical purposes or in crop production and agri-food systems for non-phytosanitary purposes

The World Health Organization produced clear guidelines on the use of medically important antimicrobials in food-producing animals in 2017. Among the recommendations, the [WHO Guidelines](#) called for:

1. an overall reduction in use of all classes of medically important antimicrobials in food-producing animals;
2. complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion; and
3. 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 [glossary in the WHO Guidelines](#) provided definitions of what is meant by “medically important antimicrobials” or “critically important antimicrobial” in human medicine, and distinctions of the use of antimicrobials in food-producing animals for growth promotion, disease prevention, or treatment (or therapeutic) use. By contrast, the framing of this second target is confusing. The Manifesto language refers to “medically important antimicrobials for human medicine,” but the explanation in the Appendix for Target 2 refers to zero use of the much narrower category of “critically important antimicrobials,” a subset of medically important antimicrobials. Regarding intended purpose of use, the Manifesto refers rather opaquely to non-veterinary medical purposes, while the Appendix describes differences in terms of growth promotion, prophylaxis, and metaphylaxis.

The Appendix makes reference to three sources for this Manifesto guidance:

1. WOA’s recommendation to “urgently prohibit the use of Highest Priority Critically Important Antimicrobials as growth promoters”;
2. the Codex general principles on foodborne AMR taking into account risk analysis and consideration of the WHO’s Critically Important Antimicrobial List; and
3. finally the exhortation of the Global Leaders Group on AMR to end the use of medically important antimicrobials for growth promotion, but only limiting “antimicrobial prophylaxis and metaphylaxis in animals and plants to well-defined situations, with a goal of markedly reducing use and ensuring that all use is performed with regulatory oversight and under the direction of an authorized prescriber.”

The Global Leaders Group on AMR’s attention to crops follows growing concerns of antibiotic and antifungal use in plant management guidelines. A [study by the intergovernmental agency, CABI](#), of agronomic advice provided to smallholder farmers discovered a surprising frequency of antibiotics being recommended in the management of crops—almost 10% of plant management recommendations for rice in one region involved use of an antibiotic. However, the reliance on regulatory oversight and particularly authorized prescribers may not address the resource-limited settings [where veterinarians and their services may be in short supply](#).

The World Organisation for Animal Health’s recommendation to prohibit urgently the use of Highest Priority Critically Important Antimicrobials as growth promoters is nowhere near ambitious enough if the goal is to genuinely tackle the overuse of antibiotics in farming. Stopping there, such a recommendation would leave much of the use of antibiotics as growth promoters and for routine preventative use unaffected. Of note, the World Organisation for Animal Health’s more restrictive guidance on families of antibiotics considered critically important for both human and animal health does not receive mention. These would include fluoroquinolones as well as third and fourth generation cephalosporins. For these two classes of antibiotics, plus colistin (considered a last-line antibiotic in human medicine that was reclassified in 2016 to the WHO’s list of Highest Priority Critically Important Antimicrobials), the [OIE List of Antimicrobial Agents of Veterinary Importance](#) recommends that these antibiotics:

- Not to be used as preventive treatment applied by feed or water in the absence of clinical signs in the animal(s) to be treated;
- Not to be used as a first line treatment unless justified, when used as a second line treatment, it should ideally be based on the results of bacteriological tests; and
- Extra-label/off label use should be limited and reserved for instances where no alternatives are available. Such use should be in agreement with the national legislation in force; and
- Urgently prohibit their use as growth promoters.

We are disappointed that the clearest guidance—that of the [WHO's 2017 Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals](#)—also receives no mention at all. Its recommendations for an overall reduction in use of all classes of medically important antimicrobials in food-producing animals as well as “complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion” and “for prevention of infectious diseases that have not yet been clinically diagnosed” would have offered needed clarity in the guidance for Target 2.

Target 3: Ensuring that ACCESS group antibiotics comprise at least 60% of overall antibiotic consumption in humans by 2030.

This third target focuses on the use of antimicrobials in the healthcare delivery system. Focusing on the percentage of antibiotic consumption in the ACCESS group is one way of triangulating in on more appropriate stewardship of these drugs. Importantly, between 2000 and 2015, the consumption of WATCH antibiotics in low- and middle-income countries climbed by 165%, much faster than in high-income countries. However, a single ACCESS metric may not address other important dimensions of this challenge, such as overall volume of use of antimicrobials used, nor recognize the underuse or lack of access to essential antibiotics. It is hard to gauge whether this target standing alone will achieve its aim of improving antibiotic stewardship. So we should consider complementary measures that recognize the reality of low- and middle-income countries,

including underuse or lack of access to effective antimicrobials. After all, the [Lancet GRAM study](#) estimates that 1.27 million people died of bacterial AMR in 2019, but the numbers dying from various infections amenable to antimicrobial treatment also are considerable. One study ballparked the [death toll from lack of access to antimicrobials for treatable infectious diseases](#) at 5.7 million each year. Benzathine penicillin G—an antibiotic key to treating streptococcal sore throat and preventing rheumatic heart disease—has faced [repeated global shortages](#). Yet at least 33 million remain at risk and over 300,000 lives are lost each year from [rheumatic heart disease](#).

We support the Oman Ministerial efforts to rally country-level support, both for advancing much needed progress towards addressing AMR and for setting targets by which countries might be held accountable. However, these targets must reflect local context, build upon data that are publicly transparent and available, and be commensurate with global resource commitments that make feasible their accomplishment.