BRIEFING NOTE

THE GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE AT A CROSSROADS: INSIGHTS FROM THE WHO'S COMPREHENSIVE REVIEW

Table of Contents

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ReAct

Introduction

In September 2021, the World Health Organization released its Comprehensive Review of the Global Action Plan on Antimicrobial Resistance (GAP AMR). Coming amidst a pandemic that has put antimicrobial stewardship to a global stress test, the recommendations of the Comprehensive Review could not provide a more timely and critical wake-up call that the global health community must more effectively address the challenge of antimicrobial resistance.

A Tripartite framework for the Monitoring and Evaluation of the Global Action Plan on Antimicrobial Resistance committed to such a review: "An independent assessment will take place within the first five years of the GAP implementation, concentrating on the lessons learned at the country, regional and global levels. It should inform revisions to the GAP. From the fifth year, an independent evaluation will assess the impact and value for money and identify opportunities to increase impact." Paragraph 4.1 of World Health Assembly resolution 72.5 in 2019 provided the mandate to conduct a comprehensive review of the GAP AMR. Both ReAct and the Antibiotic Resistance Coalition had called upon WHO to follow through on a five-year review. Six years after the adoption of the WHO GAP AMR, it also follows a similar FAO evaluation taking stock of its contribution to the GAP AMR.

The goal of the Comprehensive Review was to enable WHO and key stakeholders to enhance the ongoing implementation of the GAP AMR, by documenting the "successes, challenges, best practices" and "lessons learned and recommendations" to improve the global implementation of the GAP AMR.

The Review was primarily conducted through the lens of WHO's activities and structured its findings mainly around the five strategic objectives and related operational issues. While the Review noted several key strengths in GAP AMR implementation, it also documented missed opportunities and shortcomings.

The Comprehensive Review noted gaps in the five strategic objectives outlined in the GAP AMR. It concluded that the greatest improvements were seen in focusing on One Health arrangements and preparing National Action Plans (NAPs), but the least progress was made on infection prevention and control in human health and optimizing antimicrobial usage in animal health—key pillars for One Health action and country-level NAPs on AMR.

The Comprehensive Review identifies critical weaknesses not only in implementation of the WHO's GAP AMR, but also in the efforts to monitor and track its activities. The lack of a detailed workplan, need for greater coordination with international and national partners, slow progress on establishing an AMR global governance structure, lack of coordination across these structures, and lack of progress in mobilizing financial resources have impeded the GAP AMR implementation globally.

The review approaches the analysis based on the five strategic objectives, but their findings reveal cross-cutting challenges across all five pillars. This briefing note brings together the eight cross-cutting issues that have slowed progress on the GAP AMR agenda across all five strategic objectives.

I. Global Governance Challenges

The AMR Governance structure has not come together in a way that engages the breadth of international agencies that must be enlisted, mobilizes financing required for carrying out its work, nor ensures the necessary accountability to deliver on the GAP on AMR. It needs to be revised.

The global AMR governance structure comprises mainly of the Tripartite agencies – WHO, FAO and OIE – along with involvement of UNEP. This structure neglects other international and UN agencies, such as the UNDP, UNICEF, and the World Bank, to name a few, that have a stake in the multisectoral issue of AMR containment and can provide technical and financial resources. The Interagency Coordination Group (IACG) on Antimicrobial Resistance recommended constituting a One Health Global Leadership Group (GLG) on AMR; an Independent Panel on Evidence for Action against AMR; and a multi-stakeholder partnership platform to address the breadth of sectoral interests in AMR governance.

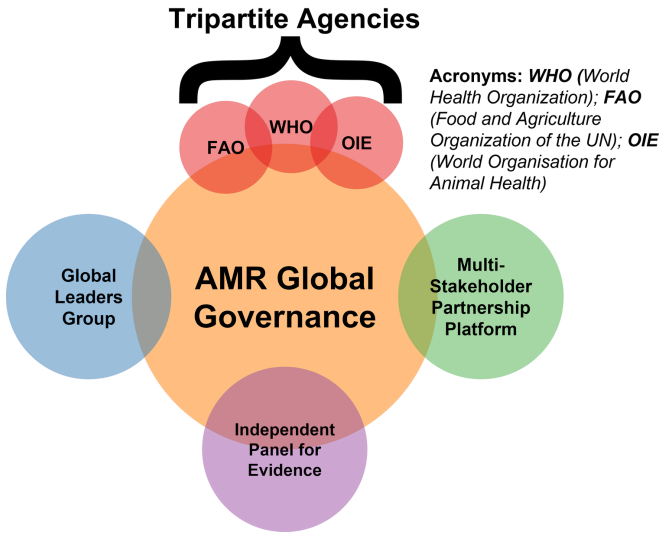


Figure 1: The UN Environment Programme (UNEP) still does not figure as an equal partner alongside the Tripartite Agencies in AMR Global Governance.

There has been a slow ramp-up of AMR global governance. The Interagency Coordination Group on AMR's recommendations in 2019 called for a Global Leaders Group, an Independent Panel for Evidence and a multi-stakeholder partnership platform. The WHO's Comprehensive Review stated that "it is difficult to assess details of how [these groups] interact among themselves and with other mechanisms, and the anticipated cost, it does seem that there could be a risk of the global governance and coordination mechanisms being too cumbersome, bureaucratic and costly." [S43, pg xiii]

The Comprehensive Review found that the progress on putting into place AMR global governance structures remains slow, with the Independent Panel and multi-stakeholder partnership platform yet to be operationalized. It also observed the lack of clarity on how these governance structures would fit together or work in connection with existing structures. The Review highlighted concerns over the mobilization of resources needed to sustain the global AMR efforts, noting how the Global Leaders Group (GLG) had fallen short of respondent expectations in identifying such financing. The Review noted civil society concerns over the lack of transparency of the Global Leaders Group's deliberations: "…while the priorities document had been published, there had been no public input or transparency and there was no connection to the Tripartite's M&E Framework."

There is much to be done to achieve the governance goals set out in the GAP AMR and subsequent efforts, such as the IACG recommendations. The creation of the GLG was a welcome step, but it remains captive to the Tripartite agencies. To be effective, the GLG must both be seen as holding the Tripartite agencies accountable and also making a compelling case, based on benchmarking that progress, for greater financing to advance that mission. The proposed terms of reference for the Independent Panel on Evidence for Action against Antimicrobial Resistance neither make it independent of the Tripartite agencies, nor is it yet operational. The proposed Multi-Stakeholder Partnership Platform is rife with design issues that threaten its potential effectiveness to mobilize constituency support for the GAP on AMR and to take action.

II. Access vs Excess in Healthcare

Only by addressing access and not just excess use of antimicrobials will there be confidence that the GAP on AMR is meant to benefit all peoples, including those in low- and middle-income countries (LMICs).

Although antimicrobial overuse is often identified as the key driver of AMR, inadequate access can contribute not only to higher risks of emergent AMR but also to higher morbidity, mortality and loss of livelihoods across human, animal and plant health sectors. While drug-resistant infections are responsible for an estimated 700,000 deaths annually, the toll from lack of access to effective antimicrobials for treatable infections exceeds 5.7 million.

The Comprehensive Review highlighted civil society concerns that WHO's Division of AMR might play a greater role in advancing antimicrobial access. Missed opportunities include the lack of access to benzathine penicillin, which imperils over 40 million people in need for prophylaxis for rheumatic heart disease, and the shortage of liposomal amphotericin-B needed to treat a surge in cases of mucormycosis following the second wave of COVID-19 in India. Intervention from the Indian government led to ramping up of local production to overcome this shortage.

The Comprehensive Review further notes that the GAP AMR emphasized the issue of antibiotic overuse in human and animal health sectors, while overlooking the issue of antimicrobial overuse for crops and plant health. A CABI study found that in the South and East Asia region, agricultural advisors regularly suggested antibiotics for rice crop problems (7.4% of the recommendations for this crop). This could potentially have accounted for the use of 63 tons of streptomycin and 7 tons of tetracycline use annually.

Though work on a Global Development and Stewardship Framework on AMR began in 2016, the WHO conceded in the Comprehensive Review that the plans to proceed have been abandoned, with the expectation that they would be covered under the proposed pandemic treaty.

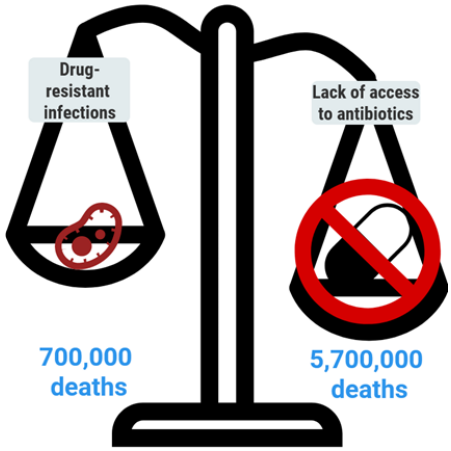


Figure 2: Today lack of access to effective antibiotics contributes to greater mortality than drug-resistant infections. [1,2]. By 2050, if unchecked, up to 10 million people may die of drug-resistant infections in 2050, more than the number of deaths from cancer each year now.

Fulfilling this expectation, however, will be challenging. The G20 Panel on "A Global Deal for Our Pandemic Age" opted to exclude "other investments that will contribute to resilience against future pandemics while benefiting countries in normal times," including antimicrobial resistance. The justification provided in the G20 report was that "while there is some overlap and synergies between pandemic prevention and preparedness and AMR containment, AMR requirements for both animal and human health are relatively distinct." If the promise of the Global Development and Stewardship Framework on AMR is to be covered in the proposed pandemic treaty, the synergy between investing in pandemic prevention, preparedness and AMR will need to be emphasized, not excluded (see Section VIII in this briefing).

Respondents informing the Comprehensive Review flagged that "there are also concerns that the GAP AMR and its implementation may be focusing more on excessive use of antimicrobials rather than ensuring access to appropriate antibiotics when they are needed." At the same time, as the Antibiotic Resistance Coalition has noted, even where AWaRe measures are adopted, the quantity of some classes of antimicrobials used in food systems in these same countries may exceed that used for human medicine.

III. Need for One Health Approach

The Tripartite Agencies (WHO, FAO and OIE) must collaborate to curb antimicrobial use not just in healthcare delivery, but in food systems and the environment. A truly One Health approach requires engaging other key international agencies beyond the Tripartite (WHO, FAO and OIE), including the UN Environment Programme

The One Health approach undertaken by the Tripartite agencies has focused moreso on human and animal health, but according to the Comprehensive Review, concerns had arisen that this approach "excludes important areas, such as plant health, food production, food safety and the environment." The need to expand the Tripartite to a Quadripartite Plus structure by engaging the UN Environment Programme (UNEP) and other UN agencies as core partners is repeatedly noted in the Comprehensive Review as a step towards operationalizing the One Health approach to contain AMR. This finding echoes a longstanding position, advanced by the Antibiotic Resistance Coalition, for inclusion of UNEP alongside the Tripartite agencies in the One Health response to tackling AMR.

The WHO's role in lifting up human health concerns in the One Health context has not met with success when it came to securing adoption of the WHO *Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals*. In 2017, these guidelines, not yet fully embraced by FAO and OIE, called for among other measures "complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion." In fact, in the most recent OIE survey on antimicrobial use in food animals, 42 out of 160 countries, or over a quarter of the respondents, reported that use of antimicrobials for growth promotion in food animals was still legally allowed.

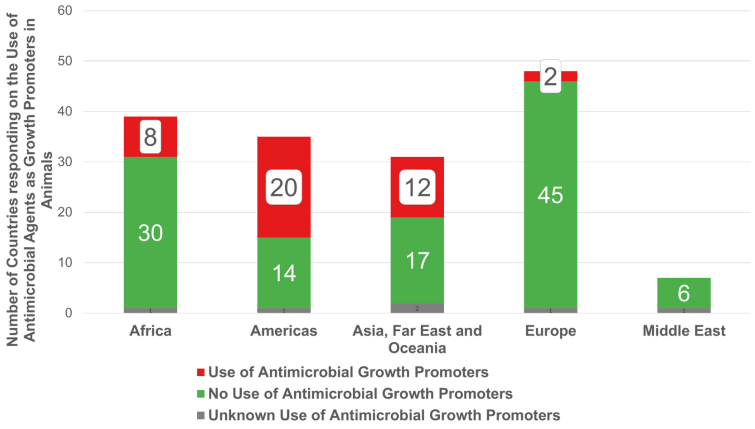


Figure 3: In the World Organisation for Animal Health's most recent report, forty-two countries report allowing use of antimicrobial growth promoters. The WHO's 2017 *Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals* recommended complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion. However, countries are still using medically important antimicrobials like colistin, tetracyclines, and amoxicillin for growth promotion.

One of the areas in which the Review has noted the greatest change from baseline levels is in the recognition that the NAPs should be rooted in multisectoral coordination, which underlies the One Health approach. Countries with pre-existing One Health arrangements were observed to have leveraged the approach better for AMR containment issues. However, the Review does note that progress in these fields may be fragile, and "could be undermined if there were changes in circumstances." The strategic framework for One Health, expected to be launched in early 2022, being finalized by the Tripartite and UNEP, is also expected to improve the One Health coordination between the involved agencies.

IV. WHO Collaboration with Partners

A coordinated approach enlisting international agencies and with meaningful engagement of civil society organizations is necessary to strengthen the One Health response to AMR.

As called for in the UN IACG recommendations, the GAP on AMR will require coordinated efforts, both "through UN Development Assistance Frameworks and ensuring a whole-UN approach to antimicrobial resistance" and also "systematic and meaningful engagement of civil society groups and organizations as key stakeholders in the One Health response to antimicrobial resistance at global, regional, national and local levels…."

The Comprehensive Review, however, observed that with respect to WHO's collaboration with partners beyond the Tripartite agencies and UNEP, "The important roles of other multilaterals and UN agencies in responding to AMR are largely overlooked in the GAP AMR and in progress reports…Similarly, there is little systematic progress reporting of the contribution of other sectors including civil society and the private sector." Civil society representatives contrasted the annual engagement in World Antimicrobial Awareness Week with the more sustained, year-round involvement seen in other areas from hand hygiene to vaccination and tobacco control. The Comprehensive Review shared concrete strategies on how WHO could enlist civil society more effectively in efforts to implement the GAP AMR:

- Holding dialogues between WHO experts and civil society organizations on priority issues in AMR – need for safe spaces for civil society and LMIC voices
- Involving civil society in processes to set indicators for monitoring and benchmarks for accountability
- Promoting bottom-up innovation as in antimicrobial stewardship and access initiatives at the community level and in healthcare delivery
- Enlisting civil society in mobilizing for campaign action, behaviour change and greater financing of AMR efforts

The UN Interagency Coordination Group on AMR's recommendations had called for "provision of political, financial and technical support for civil society organizations to enhance their engagement, including for work with governments while keeping their independence." Civil society representatives conveyed that: "We recognize the need for WHO to conduct this in a way that involves all stakeholders, but as in other areas where significant financial conflict of interest exists, we hope that WHO can go the extra mile in creating separate, safe space for the voices from LMICs and civil society to share their inputs."

More recently, the proposed structure and governance for a Multi-Stakeholder Partnership Platform on AMR has stirred concern that these take-aways from the Comprehensive Review have not been heard. The proposed design of the platform requires consensus to act and makes the private sector--whose financial interests may be at stake--a part of every consensus in the Platform. The ambition of the Platform seems more focused on recruiting 200 stakeholders than building a coalition of the willing, providing them the "political, financial and technical support" to take action, and lifting up the voices from civil society and low- and middle-income countries which may not otherwise be heard. Finally, the Platform calls for accountability to the Directors-General and the governing bodies of the Tripartite agencies when, in fact, the Platform should be empowered to hold the Tripartite and other implementing agencies accountable for meeting milestones and making progress on the global AMR agenda.

V. Beyond the Industry Roadmap to Innovation

AMR global governance must engage all stakeholders, but in so doing, resist the undue influence of those with financial conflict of interest.

As the UN IACG mentions, "civil society groups have a particularly important role to play in … ensuring transparency of governance and monitoring" and a "lack of transparency" is a "significant barrier to advancing research and development related to antimicrobial resistance."

The Comprehensive Review highlighted civil society concerns over industry influence over AMR governance. CSOs noted that focusing on industry apprehensions of insufficient reimbursement might limit access to newer antimicrobial products. Prioritizing industry-driven demands for greater returns could price newer antimicrobials out of reach of low- and middle-income countries, which experience the bulk of infectious disease burden globally. Ensuring fair returns on public investment and financing of antibiotic R&D and procurement is key. An example of how these concerns have played out surfaced in how the AMR Action Fund, a billion-dollar industry effort to support promising antibiotics through the clinical testing phase to market, has been managed. Many of these promising antibiotics were brought forward as a result of public funding, but an industry-run initiative, like the AMR Action Fund, does not have the same level of public accountability for conditions for access and stewardship as the proposed joint WHO-European Investment Bank's proposed investment fund that it displaced might have had. The practices of agricultural companies that have relied on the use of antimicrobials for production purposes, such as growth promotion, were also highlighted as a point of civil society concern in the Review.

However, there has also been some positive progress in the area of innovation. The development of the AWaRe classification as part of WHO's Essential Medicines list, the identification of priority pathogens as well as critically important antimicrobials in human medicine, target product profiles for antimicrobials and diagnostics, and monitoring of the antibacterial R&D pipeline were notable steppingstones. Still, most of these efforts have focused on developing newer antimicrobials, rather than addressing the unmet needs for diagnostics and vaccines, which would reduce the selective pressure on using these drugs. Initiatives such as the fledgling SECURE proposal to expand sustainable access to antimicrobials, need to be augmented to ensure that an end-to-end approach is devised to ensure sustainable access not only to newer antimicrobial products, but also to older agents that have limited availability or that suffer from frequent supply chain failures.

VI. Monitoring for Accountability

Over five years after the adoption of the GAP on AMR, benchmarking progress toward clear milestones is missing but critical, both to gauging the effectiveness of global and national efforts and to making the case for financial support.

In conducting the Comprehensive Review of the GAP AMR, the evaluation team noted, "It is very difficult to assess overall progress towards outcomes as these are not clearly defined…Unlike other Tripartite organizations, such as FAO, the WHO Secretariat lacks a detailed workplan for its own contribution to the GAP AMR." The review highlights the fact that while it is important to track the progress of the GAP AMR, progress towards a comprehensive M&E is hampered by a "lack of a shared understanding as to what the expected outcomes of the GAP AMR are and what would constitute success." This challenge is compounded by the WHO's failure to track systematically the outcome indicators outlined in the Tripartite M&E framework.

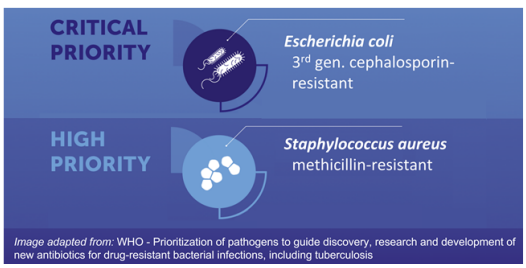
The Comprehensive Review also takes a critical look at the Global Leaders Group's priorities document and key performance indicators. The Comprehensive Review report noted, "The brief priorities document is not clear on a number of issues including how the priorities and plans to monitor progress towards them fits with the GAP AMR and its M&E framework.

Indeed, the priorities document simply gives titles of key performance indicators without defining them in detail or explaining how data on them will be collected and reported or whether baseline data exists or not."

The Tripartite M&E framework has yet to be operationalized with routine and transparent release of indicator data that could help measure progress against milestones. Among indicators to measure progress towards SDG goals, there is only one AMR-specific indicator focusing on stewardship. Members of the Antibiotic Resistance Coalition have called for another AMR-specific indicator to track access to antimicrobials to complement the focus on stewardship.

Data from the Tripartite AMR Country Self-Assessment Survey (TrACSS) have provided useful insights into progress on GAP AMR, as perceived by a country's policymakers. However, these efforts would benefit from greater external benchmarking against objective data collected. The value of such benchmarking became clear when countries overestimated the proportion of healthcare facilities with basic water supplies, basic hand hygiene and functional sanitation facilities. External reference benchmarking with UNICEF helped to spot this overreporting.

In 2020, the SDG indicators finally began tracking AMR (indicator 3.d.2). Countries now submit data on two drug-resistant pathogens.



The SDGs could better track access to the antibiotics needed to treat these drug-resistant infections through the SDG indicator on access to relevant essential medicines (indicator 3.b.3)

AWaRe

ACCESS:	1. Gentamicin 2. Amoxicillin 3. Procaine benzylpenicillin or Benzathine benzylpenicillin
WATCH	1. Ceftriaxone
RESERVE	*No antibiotics such as, linezolid for MRSA, are being tracked*

VII. AMR Financing and National Action Plans

Renewing National Action Plans must come with adequate financing or support if we are to make progress on AMR.

The Comprehensive Review mentions that the GAP AMR has served as an important, central document around which to develop national strategies. This "awareness of AMR globally…has largely not been translated into increased financial resources…not least because there is no clear purposive plan of action." Several of the GAP AMR objectives remain hamstrung by a relative lack of financial and human resources needed to implement and monitor related activities. The Review particularly identified the lack of financial resources as a limiting factor for raising awareness (WHO GAP AMR Strategic Objective 1) and infection prevention and control (WHO GAP AMR Strategic Objective 3).

While the Review also places some onus on Member States to designate more funds towards AMR, "relatively little has been done" by WHO to make the economic case of investment, even though this is central to one of the five Strategic Objectives under the current GAP AMR. Though the WHO has recently launched a costing and budgeting tool for NAPs on AMR in October 2021, there remains limited information collected to enable tracking such efforts at the country level. This is of particular concern given that TrACSS data reveal that only one in five (27/136) countries have been able to identify funding sources to support implementing their NAPs fully. Nearly 40% (54/136) of countries reported not having a budgeted operational plan for their NAPs. The Comprehensive Review notes that "while some organizations have done work on the economic case globally, this has not been used to advocate for or track global resources available to respond to AMR or to provide guidance and support for countries in terms of identifying resources available to their national action plan."

The WHO's costing tool, which responds in part to these concerns, offers countries with an approach to assess investment needs, but does not make up for "developing a tool or tools which allow prioritization of responses, particularly in contexts where resources are limited." There also needs to be political will to commit to the identified needs, and here again is where the lack of effective engagement with other constituencies, notably civil society, impedes effective progress on AMR. The role of other UN agencies from UNEP to UNICEF and UNDP, donors, multilateral agencies, and national and international civil society partners in mobilizing resources to support the AMR activities warrants emphasis in the GAP AMR. Securing buy-in from a wider group of stakeholders would further encourage synergies with AMR-sensitive interventions in other sectors, from WASH interventions to vaccination, thereby allowing both sectors to co-benefit from such interventions.

The establishment of the Multi-Partner Trust Fund (MPTF), launched by the WHO, FAO and OIE in 2019, was a welcome move. However, it has remained poorly funded, which has limited its effectiveness. The Review notes that despite the initial five-year budget called for mobilizing US$70 million, it had received around US$15 million (now just under $20 million), and most of this budget has been used for national-level activities of the Tripartite organizations.

VIII. Pandemic Preparedness & Prevention & AMR

COVID-19 provides WHO an unprecedented opportunity to find synergy and support for emerging diseases, including drug-resistant infections.

The global impact of the COVID-19 pandemic provides several lessons and opportunities from which efforts to address AMR might benefit. In mitigating the COVID-19 threat, there have been gains made in infection prevention and control, awareness of the One Health approach, ramping up diagnostic testing, and expanding vaccination to countrywide populations, which may have indirect benefits on tackling AMR at the national level. While COVID-19 has disrupted routine healthcare delivery and displaced resources that would have benefited AMR containment efforts, it has also provided a window of opportunity to root AMR in the unprecedented scale-up of global efforts to address pandemic preparedness, prevention and response.

The COVID-19 pandemic has reset the pace by which new diagnostics, therapeutics, and vaccines have been brought to market. It highlighted the importance of being able to scale up diagnostic testing, at the point-of-care, using affordable technologies, as a critical part of the public health response to contain the spread of the pandemic. Therefore, the Comprehensive Review recommended that the WHO should review how to sustain the advancements made in infection prevention and control during the COVID-19 pandemic era and harness them to improve AMR and antimicrobial use as the immediate threat of COVID-19 subsides.

In a wider context, it is expected that the negotiations on the pandemic treaty should also incorporate effective measures on antimicrobial stewardship, equity and access. There needs to be sustained advocacy to ensure that AMR is considered as one of the facets of pandemic prevention and control efforts, given the substantial overlap and synergies in the efforts. While no one is suggesting that tackling AMR in the human, animal, plant and environmental sectors is the same as stopping the next COVID-19 pandemic, failing to piggyback such investment into the common infrastructure to do both would be a huge, missed opportunity. Such missed opportunities are exemplified by the G20 panel report, "A Global Deal for Our Pandemic Age," that called for committing US$15 billion in pandemic prevention and preparedness, an estimate that failed to bundle the budgetary needs for AMR containment.

Whether a WHO convention, agreement or other instrument is taken up to address pandemic preparedness and response, such discussions should consider how such investments can pay double dividends by also addressing AMR. In its briefing for the 74th World Health Assembly in May 2021, the Antibiotic Resistance Coalition flagged such an opportunity in the transition of the Global Polio Laboratory Network. To work towards polio eradication, the Global Polio Laboratory Network (GPLN), a network of more than 140 laboratories in 92 countries, was established. As polio has been locally eradicated, environmental surveillance for poliovirus (notably sewage surveillance) has been important for rapidly responding to outbreaks. Environmental surveillance has been increasingly used for COVID-19, and there are calls for public health authorities to use low-cost sewage surveillance for antimicrobial resistance. The GPLN has developed in-country lab capacity that has expanded to other diseases. Prior to COVID-19, GPLN staff had already reported spending 30% of their time working on non-polio efforts. These staff have overlapping technical expertise for surveillance of viruses such as measles, rubella, rotavirus, yellow fever, and Japanese encephalitis. With the pandemic, the GPLN has provided support for COVID-19 case detection and laboratory testing. A cornerstone to future pandemic preparedness will be to build on existing infrastructure to support an effective global, integrated surveillance system, one in which AMR should be a key component.

The findings of the Comprehensive Review of the WHO GAP on AMR provide a timely and much needed account of where WHO has made gains and where it has fallen substantially short on meeting the expectations of the Global Action Plan on AMR. Member States should review closely the recommendations put forward in this report, and as promised in the Tripartite's Monitoring and Evaluation Framework in 2019, concentrate on what lessons might be learned as well as "assess the impact and value for money and identify opportunities to increase impact." This may require both course corrections and even revisions to the Strategic Objectives of the Global Action Plan. It is time that awareness is matched by action, that adopting GAP AMR and NAPs come with financing, and that progress is met by accountability to measurable milestones.

Launched in May of 2014 at the World Health Assembly, the Antibiotic Resistance Coalition (ARC) is comprised of more than 25 leading civil society organizational members. This policy briefing was prepared by the ReAct Strategic Policy Program, which serves as the Secretariat of the Antibiotic Resistance Coalition. Learn more about ReAct - Action on Antibiotic Resistance and the Innovation + Design Enabling Access Initiative and subscribe to the ARC Newsletter, a free newsletter put out by the Antibiotic Resistance Coalition.