EXECUTIVE SUMMARY

The emergence and spread of antimicrobial resistance (AMR) represents a grave challenge to global health. In 2019 alone, AMR caused 1.27 million deaths.

Governments have made a series of commitments to act against AMR, for instance in the 2015 Global Action Plan (GAP) on AMR and the 2016 UN Political Declaration on AMR. Despite this recognition of AMR, competing health priorities and lack of resources, particularly in countries with high rates of poverty, have impeded progress towards these commitments. The non-binding nature of the commitments and the lack of concrete targets and indicators have also acted as barriers to their fulfilment.

The multiple ongoing pandemic prevention, preparedness and response (PPR) initiatives, which include the negotiations for a Pandemic Accord, amendments to the International Health Regulations, and the creation of the World Bank-hosted Pandemic Fund, among others, feature AMR with varying degrees of prominence. There are significant overlaps between PPR initiatives and the response to AMR. Both global challenges call for international solidarity rather than nationalistic measures; inclusive governance and robust financing mechanisms; expanded surveillance and laboratory capacity; significant investments into human resources and infrastructure for healthcare delivery; and improved access to existing and new medical tools.

In view of these overlaps, ongoing PPR mechanisms offer a promising pathway to complement and cement—but not replace—pre-existing commitments on AMR and advance progress towards their fulfilment. The global response to AMR can benefit from PPR initiatives in the following spheres:

1. Governance and Funding

Incorporating measures to address AMR within PPR processes would be feasible and efficient. Such integration, if achieved through a negotiation process that centres the most-affected communities and establishes fair and inclusive governance structures, could meaningfully advance the global fight against AMR by allotting resources, establishing concrete objectives and binding obligations for nations, and ensuring that low-resource communities receive the technical and financial support they need from high-income countries.

Financial pressures in the face of multiple competing health priorities have been the biggest hurdle to meaningful action on AMR. This is reflected in the status of National Action Plans (NAPs), identified by the GAP on AMR as being essential in the fight against AMR. Not all countries have formulated such plans, and among those that have, only one in five has identified funding to finance their implementation.

Specific efforts to address AMR stand to benefit from their inclusion in financing mechanisms within PPR initiatives, even if such financing may be insufficient or at times ill-adapted to the scale and nature of efforts needed.

2. Surveillance

There is a dire need for strengthened and better-coordinated surveillance and laboratory capacities for drug-resistant infections and other potential pandemics alike. PPR negotiations can support harmonised, multisectoral approaches to pathogen surveillance and data sharing, and establish concrete obligations and measurable indicators for strengthening laboratory capacity, in ways that are mutually beneficial for PPR and addressing AMR.
### 3. Infection prevention and control and antimicrobial stewardship

Infection prevention and control (IPC) and antimicrobial stewardship (AMS) are key elements of slowing the emergence and proliferation of AMR. The need to strengthen infrastructure and capacity for IPC and AMS activities, already recognised to an extent in some PPR initiatives, should be coherently and specifically emphasised across all such initiatives, and should be accompanied by financial and technical support to low- and middle-income countries (LMICs) together with specific and measurable targets.

### 4. Access to medical tools

Access to vaccines, diagnostics and medicines animates several PPR discussions. It is also an essential part of the response to AMR, which is often hamstrung by lack of predictable and sufficient access to existing and recently developed medical tools in LMICs and inadequate research and development (R&D) of new tools. PPR negotiations represent an opportunity to put in place provisions that can address these access barriers through the systematic collection and sharing of information about access to medical tools for AMR; pooled procurement of these tools to overcome the limited demand from individual countries; diversification of manufacturing to improve resilience of supply chains and bring prices down; and promotion of open and collaborative R&D with access, affordability and transparency conditions embedded in R&D investments.

### 5. One Health

A “One Health” approach that takes into account the interdependence of humans, animals, plants and the environment is a key component both for PPR and tackling AMR. Guided by a One Health approach, PPR initiatives should define standards to limit pharmaceutical and hospital discharges into the environment and reduce the non-human use of medically important antibiotics. Concurrently, they should provide financial and technical support, especially to LMICs, to implement these standards.

### Introduction

Antimicrobial medications such as antibiotics have saved millions of lives since they were first developed in modern form in the first half of the 20\textsuperscript{th} century. But bacteria, viruses, fungi, and other microbes are always changing to ensure their survival, and some have adapted so well that drugs commonly used to prevent or kill them are no longer effective. These microbes cause drug-resistant infections, and their ability to survive medicines used against them is called AMR.

Recognising the public health impact of AMR, in recent years governments have committed to a series of measures to address AMR, most notably in the 2015 GAP on AMR. However, these commitments have not always translated into action at the pace or scale required due mainly to competing priorities and the financial constraints governments, particularly in LMICs, are faced with.

AMR has also been included in multiple global PPR processes. These processes offer synergistic, practical means by which to strengthen mobilisation against the ongoing and escalating public health menace posed by AMR – which has been a medical priority for Médecins Sans Frontières/Doctors Without Borders (MSF) for many years given the current and prospective extent of AMR’s health toll, its disproportionate impact on humanitarian settings and people we treat, and its potential to undermine much of modern medical care.

This brief discusses the interrelationship between PPR and the response to AMR. In light of their overlaps, we highlight the opportunities ongoing PPR negotiations offer to make meaningful progress on AMR, particularly through binding mechanisms and better financing, and recommend concrete targets and measurable indicators on issues of mutual importance. While AMR merits inclusion and prioritisation within international agreements to strengthen PPR, such agreements alone are not sufficient to address either the current or prospective crises that AMR represents.
1. The interrelated nature of AMR and PPR

The overlap between AMR and PPR – both the pathogenic threats themselves and the structures and practices needed to prevent and counter them – is extensive. In the zero draft of the World Health Organization (WHO)-led Pandemic Accord, AMR was invoked as a “silent pandemic” and an “aggravating factor during a pandemic,” but neither of these formulations captures fully:

1) the extent to which AMR is itself already both a threat and a leading killer worldwide, with low-resource settings bearing the highest burdens of disease; or

2) the host of intersections between AMR and other infectious threats.

Bacteria such as Yersinia pestis (bubonic plague), Rickettsia species (typhus), and Vibrio cholerae (cholera) and mycobacteria such as Mycobacterium tuberculosis (tuberculosis) have caused pandemics in the past and bacterial pathogens continue to be direct pandemic threats. Many bacterial infections are preventable and/or treatable but remain a continually re-emerging affliction all around the world, and particularly in resource-constrained settings where living conditions are poor and high-quality healthcare is scarce. The development of AMR that inevitably attends this recurrent emergence impacts people in vulnerable circumstances first and disproportionately but is not geographically bounded. As resistant bacteria and fungi develop and disseminate globally, they are likely to follow an epidemiological trajectory different from the explosively dynamic ones that have characterised some pandemics like COVID but every bit as menacing and deadly.

Viral pandemics like COVID can also compound and accelerate the spread of infections from other microorganisms and the rise of resistance to antimicrobials. Viral pandemics may pose a substantial risk of hospitalisation and secondary bacterial and fungal infections, because of the virus at issue, disrupted or delayed medical care, and the use of immunosuppressive therapies. This phenomenon not only heightens risk of severe morbidity and/or mortality, but – combined with intensified use of antimicrobials, long hospital stays, overcrowding, and shortages of supplies and personnel – accelerates the emergence and spread of AMR. Indeed, all microorganisms (viruses, bacteria, fungi, parasites) can develop resistance to antimicrobials, a reality that should be front and centre in all planning for health emergencies.

Future scenarios aside, AMR is far from “silent” in the present: in 2019, 1.27 million deaths were attributable to bacterial AMR. Given the magnitude of the toll that it is already taking, AMR warrants immediate and ongoing prioritisation by governments and other global health actors. Despite the global consensus that has emerged in recent years about the threat that AMR poses, however, competing urgent health priorities and lack of resources, particularly in countries with high rates of poverty, have been a significant barrier to progress in implementing measures to counter resistant infections.

There are many measures that are urgently needed to counter AMR globally that are also key for improving prevention of and preparedness for responding to pandemics, including but not limited to:

- increasing access to quality primary healthcare and establishing community-driven contingency plans to deliver care at all stages in the surveillance, detection, or development of an outbreak;
- investing in the infrastructure and healthcare workers needed to provide care, conduct diagnosis and surveillance, and implement infection prevention and control and antimicrobial stewardship;
- investing in prevention and health promotion, including increased access to water and sanitation and expanded vaccination coverage;
- improving policies and mechanisms to ensure sustainable access to existing vaccines, diagnostics, and antimicrobials;
- increasing investment in R&D for needed medical tools and ensuring equitable access to emerging products;
- addressing environmental factors conducive to the development of resistance and transmission of infection; and
- putting in place inclusive governance and adequate and sustainable financing to structure and fund all of the above.
As a phenomenon that threatens the entire global community but disproportionately impacts people in low-resource settings, AMR also illustrates how inseparable the struggle for health equity is from the struggle against infectious pathogens and the importance of placing equity at the center of PPR planning. Governments and global health actors grappling with the lessons of COVID – and in particular with the pandemic’s outsized impact on marginalised communities and those with fewer resources – have much to learn from those already working to address AMR in low-resource settings.

**It is important to note that the “securitisation” of global health that COVID and the ensuing PPR mobilisation are accelerating is at odds with what is needed to address global health emergencies including AMR adequately and sustainably: international solidarity.** Some of the public health hazards of this approach were also made evident by nationalistic actions taken during COVID such as travel bans and suspensions of refugee resettlement efforts, delayed outbreak notifications due to trade concerns, and the hoarding of scarce, lifesaving medical tools that contributed to stark inequities in access. AMR is especially instructive in indicating the shortcomings of the “health security” framework, though, because the complex, ecological nature of the emergence and spread of resistance demands remedies that are holistic and structural in nature and attentive to all components of the One Health framework.\(^{13}\) Measures meant to simply fortify national boundaries against microbial intrusion will inevitably fail.

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**2. Integrating, but not subsuming, global commitments on AMR within international agreements on PPR**

**2.1 Governance and policy coherence across instruments**

Incorporating measures to tackle AMR within instruments and processes aimed at improving PPR is feasible, would represent an efficient utilisation of limited time and resources, and holds promise for materially advancing the fight against AMR by allotting funds for this purpose (e.g. through the Pandemic Fund) and establishing concrete objectives with binding obligations for nations (e.g. through the Pandemic Accord and/or the IHR amendments). In these ways, multilateral mobilisation around PPR could occasion some key initial steps in addressing AMR that progress past the provisional, voluntary nature of the 2015 GAP on AMR and prefigure more comprehensive commitments through other multilateral efforts focused on AMR, including the UN High-Level Meeting on the issue next year.

In 2019, the One Health Tripartite organisations (WHO, the Food and Agriculture Organization of the UN and the World Organization for Animal Health – now a “quadripartite” that includes the UN Environment Programme) – released a monitoring and evaluation framework that carried the promise of milestones by which the agencies could mark progress towards goals under the GAP on AMR.\(^{14}\) Defining fair and meaningful milestones for enacting the GAP on AMR, measuring progress against them, and making these results public is key to holding governments, intergovernmental agencies, and other global health actors accountable. PPR processes, holding out as they do the promise of increased global coordination and accountability, offer a chance to arrive at a set of binding and meaningful commitments on AMR. Such text within PPR-related agreements, however, should not be seen as replacing commitments by states through AMR-specific governance processes and should accelerate rather than delay progress toward the formulation and implementation of NAPs around the world, as called for by the GAP.

**While each government has the responsibility to respond to the threat resistance poses within its borders, given the profound differences in levels of economic development, capacity, and resources amongst nations, countries with greater means bear a greater responsibility to take action to address AMR and fill resource gaps globally.** Ideally, such fairly apportioned obligations should be assigned under binding international agreements that operationalise the principle of common but differentiated responsibilities (CBDR).\(^{15}\) Irrespective of the specific governance mechanism, however, the world will not make real headway against AMR unless the principle of global solidarity is meaningfully reflected in the structure of multilateral efforts to address resistance.
The current state of NAPs for AMR is instructive in this regard: in spite of increased global awareness about AMR, competing urgent health priorities and lack of resources in developing countries have been a significant barrier to progress in addressing this threat. NAPs are essential in the fight against AMR, but not all countries have formulated such plans yet, and among those that have, only one in five has identified funding to finance their implementation.\textsuperscript{16,17,18,19} Moreover, AMR-focused investment by global health actors has thus far disproportionately favored technical fixes like antibiotic innovation rather than preventing upstream drivers of AMR such as inadequate sanitary infrastructure or unaffordable health care.\textsuperscript{13} As PPR processes and initiatives integrate measures to address AMR, they should ensure that low-resource communities receive the technical and financial support they need from high-income countries to meet their obligations and that expectations are realistic, matched to local needs, fair, and not unduly burdensome.

Relatedly, lower-income countries and civil society must also be assured meaningful participation in the formulation and governance of PPR initiatives and negotiations, as well as the processes by which multilateral bodies such as the Global Leaders’ Group on AMR, the Independent Panel on Evidence for Action Against AMR, and the Multi-stakeholder Partnership Platform determine how progress on AMR will be measured, resources allocated, and programmes designed and implemented.\textsuperscript{20,21}

Perhaps because of the diversity of ways in which AMR affects different communities – in terms of the variety of resistant pathogens, diverse modes of transmission, and wide-ranging health effects from varied types of infections – as well as the disproportionate impact of AMR in low-resource settings with limited access to diagnosis and many competing health priorities, communities most affected by AMR do not as yet have as strong and unitary a civil society presence as other patient groups. This makes it even more incumbent upon those leading these international PPR processes to foster participation and ensure adequate and authentic involvement of affected communities.

It is essential that any international pandemic agreement:

- specify how the agreement will apply to AMR, both during and in the interregnums between other pandemics;
- specify how the One Health framework applies to all elements of the agreement;
- attend specifically to the needs of people in vulnerable circumstances in surveilling and responding to outbreaks including AMR;
- ensure inclusive governance with active participation by civil society and affected communities;
- include text that lays out specific, quantifiable, action-oriented steps countries will take to counter AMR, indicators for evaluating progress, and targets for measuring success;\textsuperscript{3,22}
- establish meaningful mechanisms for accountability and providing financial support to countries without sufficient means to implement action steps articulated, operationalising the principle of CBDR; and
- link with and clearly define its relationship to the GAP on AMR, existing AMR-related funding mechanisms, and NAPs.

### 2.2 Financing

As noted above, funding is a major barrier to the advancement of national-level mobilisation to address AMR in LMICs. While the emergence of initiatives like the AMR Multi-Partner Trust Fund – a joint funding mechanism of the UN to drive financing and support for implementation of NAPs – is encouraging, the Fund remains only partially funded, leaving many countries without any or only very little support.\textsuperscript{23,17}

Furthermore, in many places where MSF has a presence, NAPs may not be feasible without targeted support and additional resources. For instance, in the Central African Republic and South Sudan, where years of war and instability have resulted in weak healthcare systems, no NAPs have been formulated. Low-resource health systems and weak government structures are increasingly tested by conflict, climate emergencies, food insecurity, outbreaks and population displacement that demand more immediate attention. For this reason, it is essential that AMR initiatives be integrated into and prioritised within existing health programmes and that AMR NAPs are realised within broader national development agendas, particularly in resource-constrained and humanitarian settings.\textsuperscript{24,25}
Multilateral PPR agreements and financing initiatives such as the World Bank-hosted Pandemic Fund (PF) represent key opportunities to take advantage of the many synergies between PPR and addressing AMR and leverage existing aid and development agendas and global health programmes to make meaningful progress on AMR in low-resource settings. The PF, for example, has made activities related to AMR eligible for financing to the extent that “[i]nvestments in pandemic prevention and preparedness decrease the risk of infections and therefore the risk of AMR.” The first round of PF investments, indeed, focus on three priorities that are all also core elements of effective AMR NAPs: disease surveillance and early warning systems (with a specific objective to improve surveillance of AMR and antimicrobial consumption), laboratory systems, and human resources, public health and community workforce capacity (with specific references to health facilities’ ability to counter AMR through strengthened infection prevention and control).

At the same time, addressing AMR globally will require robust financing, beyond what’s likely to be integrated within funding mechanisms designed for PPR. As outlined in the GAP on AMR, NAPs need to include many elements not fully contemplated in the PF’s initial financing round, such as: AMR surveillance beyond hospitals; addressing antibiotic use in animal health and agricultural practices; immunisation programmes to deploy existing vaccines; increasing access to clean water and sanitation; measures to increase equitable access to existing and novel antimicrobials; and investment in the development of new medical tools (antimicrobials, diagnostics, and vaccines).

Questions are also arising about the governance and sustainability of the PF that have implications for its potential to help stem AMR in low-resource settings. Some in civil society have raised doubts about whether the governance of the PF is adequately inclusive of the countries that will be its primary beneficiaries or putting the PF in a position to leverage existing and effective global health programming. Moreover, while the PF states it will only receive grant contributions and only provide grant financing during “this early stage of [its] establishment,” it has also indicated an intention to ultimately mobilise new, additional resources through co-financing that include loans, credits and domestic resource mobilisation. Such an approach would be unsustainable in most contexts where MSF treats patients, and has the potential to further exacerbate inequality in the resourcing of AMR response.

AMR warrants significant global financing beyond mechanisms narrowly targeted to finance PPR, but it is welcome and appropriate that these mechanisms include AMR within their scope. Such funds should ensure, however, that countries can take advantage of synergies between existing programming/funding and AMR-related needs and that financing is not tethered to narrowly defined “pandemic” circumstances and is sustainable to support NAP formulation and implementation over the long term.

3. Key thematic areas for the development of concrete targets, at the intersection of AMR and PPR

The overlap between what is needed for effective PPR and mobilisation against AMR is extensive, but the extent to which PPR agreements will include AMR-targeted measures and which ones is as yet unclear and subject to debate. Based upon our experiences responding to infectious disease outbreaks, epidemics, and pandemics, as well as implementing an interdisciplinary and multifaceted approach to preventing and addressing drug resistance in our projects in low-resource settings around the world, MSF offers the following non-exhaustive reflections regarding key thematic areas for the development of concrete targets and potential inclusion in PPR-related instruments.

3.1 Strengthening surveillance and laboratory capacity

Effective surveillance is a core element of PPR given the need to identify pathogens of pandemic potential as early as possible and respond with appropriate public health measures to stem or mitigate infectious spread. Surveillance is likewise crucial for controlling AMR, and ongoing efforts to scale up action against drug resistance, as well as the world’s experience with the COVID pandemic, indicate that surveillance systems are in dire need of improved global coordination and strengthening, particularly in LMICs.
Multilateral PPR agreements should strengthen and support harmonised, multisectoral, One Health approaches to surveillance, data sharing, and communication in ways that mutually benefit PPR and efforts to address AMR. *Integrated analysis of data across the human, animal and environment sectors that account for all types of pathogenic threats should be a key priority, as should surveillance of antimicrobial consumption, use and access.* To the extent that PPR agreements establish new surveillance systems and infrastructure, these should build on and be harmonised with already existing programmes, including the WHO’s Global Antimicrobial Resistance and Use Surveillance System (GLASS). A global framework is also needed to ensure that any obligations to detect and report pathogen data are accompanied by strong provisions safeguarding privacy and adequately matched with equally strong rights to access to medical products or other benefits that may emerge as a result of such data sharing.35

A key building block of effective surveillance is laboratory capacity, which is essential not only to guide public health interventions and decision making at local, national, and global levels but also for providing high-quality care at the individual patient level. In many lower-resource settings, however, access to microbiological laboratories is sorely lacking. A recent network survey of 50,000 medical laboratories in 14 African LMICs, for example, indicated only 1.3% of them conduct bacteriology testing, with limited accessibility for the majority of the people in at least eight of these countries.36 Humanitarian contexts like those in which MSF operates – often amid armed conflict, civil unrest, violence, famine, and natural disasters – are particularly likely to constitute blind spots in AMR surveillance.

Struggling against the challenge of poor access to high-quality bacteriological laboratories in the contexts where we work, MSF has steadily increased our own diagnostic capacity in recent years – prioritising projects at especially high risk for AMR. A designated group of microbiology experts within MSF works on increasing access to high-quality bacteriological laboratories, norm-setting, and supporting MSF projects with tools such as guidelines, standard operating procedures, selection of tests, standardised testing protocols, and – in some cases – laboratory innovations inspired directly by project needs.37,38

Multilateral agreements present an opportunity to establish concrete obligations and measurable indicators for strengthening laboratory capacity, including obligations to provide financial and technical support for development of infrastructure and training of personnel, as well as support for the development and implementation of laboratory innovations that are adapted for impactful and sustainable use in low-resource settings.

### 3.2 Human resources and infrastructure for quality healthcare, infection prevention and control (IPC), and antimicrobial stewardship (AMS)

Access to high-quality healthcare is essential for both effective PPR and countering AMR, enabling prevention, precise detection, appropriate treatment, and recovery from infection. As a medical humanitarian organisation, MSF is committed to providing high-quality care in circumstances where it is otherwise unavailable or in short supply – which includes ensuring that the safety and efficacy of our medical interventions are promoted at all levels. As integral elements of safe and effective healthcare, IPC and AMS are both priorities for MSF, alongside other forms of prevention and health promotion.

IPC is an evidence-based approach to prevent harm caused by preventable infections – whether viral, bacterial, fungal or other – and is therefore a fundamental element of PPR. IPC prevents cross-contamination between patient, staff, visitor, and environment in any healthcare setting, and is thus also a key element for slowing the emergence and proliferation of AMR because it prevents outbreaks and reduces the number of patients in need of antibiotics. AMS is the effort to measure and improve how antibiotics are prescribed by clinicians and used by patients in order to improve patient outcomes and help minimise the misuse of antibiotics, which is a major driver of AMR.39 Given the increased utilisation of antimicrobials associated with pandemic circumstances, infrastructure and capacity for AMS should also be core to PPR.

MSF’s IPC and AMS experts provide direct support to colleagues on the ground in projects and work to continually optimise resources, guidance, and facilities that project teams use in providing care. IPC and AMS leads also train healthcare providers through the MSF Academy for Healthcare, an MSF-wide initiative that
develops and implements competency-based curricula tailored to MSF operational needs, using a learning cycle based on theoretical knowledge and workplace practice, accompanied by clinical mentoring.¹

The Academy works in collaboration with local health and higher education ministries and schools, and is designed to improve the quality of healthcare provided in MSF projects and to strengthen local health systems where healthcare human resources are lacking.

Multilateral agreements and mechanisms designed to govern and support PPR present an opportunity to build out essential infrastructure and capacity for both IPC and AMS in LMICs by allocating resources for this purpose and specifying higher-income countries’ obligations to contribute to these efforts. The PF’s inclusion in its first funding round of human resources and public health and community workforce capacity (with specific reference to countering AMR through IPC) is encouraging, as are the October 2023 Pandemic Accord negotiating text proposal’s references to ensuring “implementation of effective infection prevention and control measures” and committing “financial and technical support, assistance, and cooperation, in particular to developing countries, in order to strengthen and sustain a skilled and competent public health, health and care workforce.”³⁴ This emphasis on workforce capacity building – with specific reference to AMR - should be coherent across the different PPR policy instruments under consideration, paired with commitments to strengthen infrastructure, reflected in specific and measurable targets, and accompanied by sufficient financial and technical support for LMICs.

The PF’s first-round funding does not include efforts focused on water, sanitation, and hygiene (WASH), or vaccination – interventions that not only prevent the emergence and transmission of drug-resistant bacterial and fungal infections but prevent infections more broadly. The October 2023 proposal for the negotiating text of the Pandemic Accord does include language on strengthening WASH and strengthening health systems including primary health care but not immunisation specifically (beyond access to newly developed vaccine countermeasures). MSF’s operational experience affirms the importance not only of AMR-specific measures to prevent infection and identify and reduce transmission of pathogens – namely diagnosis, IPC and AMS – but AMR-sensitive interventions such as WASH and vaccination, preventive and health promotion measures that are also part and parcel of quality healthcare.³⁰,⁴¹

While it may not be feasible for PPR-focused mechanisms to ensure comprehensive and meaningful progress on all broadly preventive AMR-sensitive measures, within PPR processes countries should nonetheless: acknowledge the need for concrete, measurable progress in these areas; include specific and substantive commitments where possible; and commit to pursuing additional forms of multilateral action to achieve progress in areas deemed to be beyond the scope of PPR. Such action should entail commitments that advance long-term and sustainable solutions to water access and encourage investment in the development of WASH structures including sewage latrines and wastewater treatment facilities. Also needed is action to expand the global use of vaccines available for bacterial infections that can be drug-resistant and vaccines for infections that drive unnecessary antibiotic use. Meaningful expansion of global vaccination coverage will require increasing immunisation financing and strengthening capacities to ensure affordable supply, functional delivery systems and programmatic sustainability, as well as ensuring equitable access to quality-assured and affordable medical products.

3.3 Access to medical tools, existing and yet-to-be developed

Beyond the possibility of a non-viral pandemic that would itself require effective antimicrobial treatment, viral pandemics can pose a substantial risk of hospitalisation and secondary bacterial and fungal infections, thereby heightening the chances of severe morbidity and/or mortality and the need for health systems to have prompt, sustainable access to effective antimicrobials and diagnostics for these pathogens. As such, equitable and sustainable access to effective medical tools is essential for both PPR and to address AMR.

¹ Thus far MSF’s structured approach to implementing AMS has focused on hospitals, despite the fact that primary healthcare facilities are the places where the highest amount of antibiotics are prescribed and the quality of antibiotic prescriptions is sub-optimal. MSF is actively exploring tools and approaches for expanding implementation of AMS in primary healthcare settings.
Access to existing medical tools

Antimicrobials are one of the categories of drugs most prone to stockouts and shortages, an issue that impacts both high- and low-income countries and is compounded in a global health emergency. But while high-income countries are rapidly seeking ways to shore up supply chains and build domestic manufacturing capacity to ensure national health needs are met on an ongoing basis and in health emergencies, in low-resource settings the issue is more acute, underreported, and often unaddressed.  

The causes of access gaps and shortages are complex and varied, including: supply disruptions; a highly consolidated market and a limited variety of quality-assured sources; a market environment that disincentivises sustainable manufacturing of some basic existing antimicrobials; inaccurate forecasts of countries’ needs; lack of capacity for active stock management; weak procurement systems; and clinical knowledge gaps and biases. Historically, AMR-specific indicators tend to capture only one side of the challenge of antimicrobial usage – consumption and potential overuse. More robust collection of access data will be critical in informing policy and closing the access gap.

It is also the case that when new antimicrobials promising to address drug-resistant infections are introduced, there is often a significant delay in access for LMICs. Many countries are simply excluded as markets for new antimicrobials on the basis of their being economically unattractive. Scaling up access to novel antimicrobials meant to be reserved for last-line use, such as treatments for carbapenem-resistant pathogens, is particularly challenging. New drugs tend to have very high prices that are prohibitive in many countries, as well as intellectual property (IP) protections that delay the introduction of generics. Moreover, challenges to implementing AMS in lower-resource settings may also impede launch of last-line treatments in places where they are badly needed.

Access to existing diagnostics and vaccines is likewise highly inequitable globally, with massive consequences for any effort to address AMR. The COVID pandemic was illustrative in this regard: when Americans could easily obtain at-home diagnostic tests essential for infection control and were getting inoculated with newly developed vaccines in large numbers, people in LMICs struggled to gain access – even at the height of pandemic waves.

Multilateral agreements on PPR present an opportunity to put in place explicit objectives and indicators for expanding LMICs access to needed medical tools and include provisions that:

- support countries in collecting robust data on access to tools to tackle AMR;
- support diversification of manufacturing capacity and technology transfer for antimicrobials, including for active pharmaceutical ingredients, diagnostics, and other medical tools, to facilitate scaled-up production;
- improve information sharing regarding supply and forecasting across distribution lines and support countries in managing supply chains and anticipating need; and
- foster novel international pooled procurement platforms through which developing countries can opt to access antimicrobials, diagnostics, and other medical tools sustainably. Procurement mechanisms should have conditions around access, affordability, and stewardship built into their agreements, with stewardship criteria that are set in accordance with the ultimate goal of assuring access and accompanied by sufficient funding and technical support to ensure this goal is realised.

Governments and global health actors should engage with emerging initiatives such as the SECURE Antibiotic Facility, set up by WHO and the Global Antibiotic Research & Development Partnership (GARDP) with strategic input from the United Nations International Children’s Emergency Fund (UNICEF) and the Clinton Health Access Initiative, which is pioneering a set of ambitious solutions resembling those outlined above. Without a collaborative, global approach to these access challenges, no country will be insulated from the potential impacts of scarcity.
Access to prospective novel antimicrobials, yet-to-be developed

There is also a significant need for strategic investment in developing not only antimicrobials of public health importance, but diagnostics, which have been even more badly neglected in biomedical R&D to date.\textsuperscript{a} PPR agreements hold the promise of increased, public health-driven investment in much-needed innovation – though this should not come at the expense of the other thematic areas enumerated above.

Initiatives to foster antimicrobial discovery and development such as the CARB-X, private sector-driven initiatives, and the non-profit GARDP are vital but insufficient to fill the void in innovation that results from the fundamental tension between the need for restraint in antimicrobial usage, the relatively small or unknown size of markets for new antimicrobials, and the innovation system’s reliance on volume-based sales to incentivise R&D.\textsuperscript{38} MSF is concerned, however, that policy approaches to incentivise antimicrobial development currently under consideration in higher-income countries may not achieve their intended ends, fall short of what is needed to address the issue worldwide, and could even have negative unintended consequences for global access.\textsuperscript{33,34} For any R&D incentive mechanism fostered within PPR agreements, we believe repercussions for the affordability and accessibility of resulting medical tools around the world should be thoroughly considered.

Beyond economic incentives, a more open, collaborative innovation ecosystem is needed to overcome scientific bottlenecks in antimicrobial R&D, encourage clinically significant innovation, and facilitate access and development of context-specific stewardship mechanisms. Governments could help address barriers and inefficiencies in the development of antimicrobial medical countermeasures, for example, by exploring open-source compound libraries that accelerate non-duplicative drug discovery research and helping to establish sizable global clinical trial networks, including sites in LMICs.\textsuperscript{iii,iv} Multilateral PPR agreements should establish binding obligations for governments to coordinate and cooperate on R&D and build countries’ capacity to do so. As mentioned above regarding pathogen data sharing, a global framework is also needed to ensure that participation in clinical research is attended by strong rights to access to resulting medical products or other benefits – and that countries that do not host trials but need these products still have access.\textsuperscript{3}

Diagnostics innovation receives short shrift in policy discussion and resource allocation despite the facts that companion diagnostics are critical for the effective introduction of any new antibiotic and that diagnostics more generally are essential for addressing AMR. In addition to the laboratory infrastructure and trained human resources that are essential components for establishing diagnostic capacity, appropriate and readily available diagnostic tools – including those viable for use in resource-constrained settings – are critical to distinguish between bacterial and viral infections, identify pathogens, and test for susceptibility to antimicrobials.\textsuperscript{55,56,57}

If PPR agreements encourage investment in R&D for AMR-specific medical countermeasures, they should contain provisions to ensure that funding:

- prioritises investment in diagnostics, particularly technologies that are affordable, accurate, fast, user-friendly, robust and require minimal infrastructure and training to use;
- prioritises investment in antimicrobials that meet WHO’s innovation criteria and target the WHO’s global priority list of antibiotic-resistant bacteria;\textsuperscript{48,58}

\textsuperscript{a} Investment in vaccine research and development is likewise crucial. There is a pressing need for new vaccines with potential to impact AMR in developing countries and novel financing mechanisms to support vaccine development to bring candidates from discovery through preclinical and clinical testing to licensure, adoption, and implementation. See: https://www.who.int/news/item/28-07-2023-vaccines-could-avert-half-a-million-deaths-associated-with-anti-microbial-resistance-a-year

\textsuperscript{38} One example to build on is the joint natural product library effort being carried out by the National Cancer Institute and the National Institute of Allergy and Infectious Diseases.

\textsuperscript{48} Examples of such globally coordinated trials include: the WHO-coordinated Solidarity trial and the UK RECOVERY trial for COVID treatments and the SNAP collaboration focused on \textit{Staphylococcus aureus}. 
comes with conditions that ensure affordability, the widest possible availability, and diversified production of resulting new health technologies, with transparency across supply chains;\(^3\),\(^59\),\(^60\).\(^v\)

prioritises public or non-profit R&D initiatives, as these are more likely to enhance coordination and collaboration, be cost-effective and ensure resulting products are affordable and accessible.\(^61\),\(^62\)

### 3.4 Environmental factors/One Health

There is broad recognition that both PPR and addressing AMR require a multisectoral One Health approach that takes into account the interdependence of humans, animals, plants, and the environment. A One Health approach is essential for addressing multiple health risks that emerge at the human-animal-environmental interface, including not only infectious and zoonotic diseases and AMR, but food insecurity, threats from climate-related events, and others.

The COVID pandemic, caused by a zoonotic virus, drove home the importance of One Health for PPR and brought attention to the multiple ways in which changes to global ecosystems – including climate change and biodiversity loss – are hastening the emergence of new infectious threats by altering human interactions with animals and the environment. In the case of AMR, the relevance of One Health is also well established: pollution from hospital and community wastewater; effluent from pharmaceutical production; and routine use of medically important antimicrobials in intensive crop, terrestrial, and aquatic animal production are all significant drivers of resistance.\(^63\) Preventing and managing such biological and chemical sources of resistant genes and microorganisms are essential to countering AMR. Ongoing PPR-related policy discussions have, however, thus far equivocated about the precise place and characterisation of One Health within international instruments and initiatives.\(^34\)

PPR agreements should have a clearly defined One Health approach at their foundation and specify how each provision will relate to and build upon this underlying framework. In doing so, such agreements should also clarify how they relate to the GAP and NAPs, and how these in turn link to national and global environmental planning, for instance to preserve biodiversity and respond to climate change. Both PPR and the effort to address AMR globally would be materially advanced by provisions that lay out specific actions, targets and indicators to:

- define and enforce standards to reduce pharmaceutical manufacturing discharges and emissions, including by strengthening regulation and inspection systems;
- define and enforce standards for reducing non-essential use of medically important antibiotics, including for non-human purposes; and
- provide technical and financial assistance to LMICs to promote WASH to limit the development and spread of AMR in the environment as well as to reduce infections and the need for antimicrobials.

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\(^v\) Funding should come with transparency requirements, ideally including transparency on: the costs of R&D (including clinical trial costs, first and foremost), manufacturing costs, terms and conditions of R&D funding agreements and all sources of funding, prices of resulting medical tools, complete preclinical and clinical trial data, status of patents and other IP and licensing agreements, and supply and procurement agreements. On the need for clinical trial cost transparency in the US, see: MSF USA, [The Biden administration must disclose the costs of clinical trials](https://www.medicalaction.org/us/biden-administration-must-disclose-costs-clinical-trials), January 31, 2022; and Ava Alkon, Christopher Morten, and Reshma Ramachandran, “Are high-cost prescription drugs the price of innovation? Disclose the costs of clinical trials,” The Hill, April 21, 2022.
Conclusion

The ongoing processes to prevent, prepare for and respond to pandemics have recognised AMR and the mechanisms needed to respond to it in varying degrees. This attention is timely considering both the gravity of the problem and the slow progress by governments towards fulfilment of their existing commitments on AMR.

Given MSF’s extensive experience responding to infectious diseases, we believe PPR initiatives can provide a fillip to the global action against AMR by strengthening pathogen surveillance capacities; building out the infrastructure for IPC and AMS activities; and creating the conditions for better access to antimicrobials, diagnostics and other medical tools. With concrete targets, measurable indicators and commensurate financial support, these measures will complement and help implement NAPs on AMR, particularly in LMICs, in addition to aiding PPR efforts.

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