

GLOBAL LEADERS GROUP ON ANTIMICROBIAL RESISTANCE RECOMMENDATIONS TO ADDRESS THE ANTIBIOTIC PIPELINE AND ACCESS CRISIS IN HUMAN HEALTH

February 2024



Executive Summary

At its sixth meeting in February 2023, the Global Leaders Group (GLG) on Antimicrobial Resistance (AMR) held an in-depth discussion on how the world is entangled in an antibiotic pipeline and access crisis. The focus of this report is on antibiotics used for humans, though similar challenges are also faced in the animal, food and environment sectors. The pipeline and access crisis is delineated by the diminishing effectiveness of current antibiotics, limited global access to antibiotics (novel and generic), and an insufficiency in the research and development (R&D) pipeline for innovative antibiotics needed to treat drug-resistant infections. The lack of access to existing and innovative antibiotics is a contributor to the inappropriate use of antibiotics and the development of antimicrobial resistance. The GLG believes that antibiotics should be considered as global public goods, which should galvanize collective action to address the antibiotic pipeline and access crisis. While new antibiotic R&D and access incentives are being piloted and implemented, they are still in their infancy and have yet to bring meaningful impact on global access and innovation. Concurrently, there is a critical gap of diagnostics tools (new and existing) that enable appropriate clinical care, antibiotic stewardship and monitoring of resistance at different levels of the health system.

The antibiotic pipeline and access crisis requires more and predictable multi-decade funding to incentivize innovation, sustain action, and achieve results. However, funding alone is not enough. Stimulating R&D and safeguarding access to antibiotics demand a cooperative, multi-entity approach, blending the capacities of public and private sectors to maneuver through the challenges and construct resilient, equitable and sustainable access to antibiotics globally. Efforts to support the development of, and access to, diagnostics are also critical to ensuring appropriate access to antibiotics and should be considered as part of a holistic approach.

To address the antibiotic pipeline and access crisis, the Global Leaders Group is making six recommendations for global action across a range of mutually reinforcing financial and nonfinancial solutions. Together, these solutions can serve as the basis for advocacy and action in advance of the High-level Meeting on AMR in September 2024, help transform the recent G20 and G7 commitments around R&D and access into action, and catalyze collective, global action.

RECOMMENDATION 1

Working with governments, industry, and other key stakeholders, WHO should lead the establishment of global shared R&D targets for antibiotics and diagnostics for human health, with implementation roadmaps and target product profiles.

The current approach to R&D is not resulting in a sufficient number or type of innovations. The absence of clear and shared R&D targets could scatter resources and efforts needed to tackle R&D priorities and deliver novel antibiotics. There is a risk that in the absence of goals and roadmaps, best efforts will inadvertently not target public health priorities and the global burden of disease, and resources may not be mobilized due to a lack of overarching strategy. There is also a need for more precise and rapid diagnostics, preferably molecular point-of-care methods to identify infections accurately and facilitate timely and appropriate use of antibiotics in both human health and animal health. Well-defined targets could anchor a widespread ecosystem, directing research, development, and manufacturing, and facilitate funding and collaborative action.

RECOMMENDATION 2

Public and private funders should increase funding for push incentives to support the development of antibiotics and diagnostics.

To achieve a sustainable flow of new antibiotic drug candidates into and through the clinical pipeline, drug discovery and development need to be strengthened and expanded. Some studies have proposed that additional financing of \$250 – 400 million per year¹ is needed for antibiotics alone. As it can take years for low- and middle-income countries (LMICs) to have access to innovations enabled by push incentives, global access strategies should be a core part of push incentives.

¹ European Commission (2022). Study on bringing AMR Medical Countermeasures to the Market, p. 110. [Link](#)

RECOMMENDATION 3

The G7 and G20 should each play their role in establishing pull incentives to support R&D and enable access to antibiotics and diagnostics.

By themselves, push incentives for antibiotics do not provide an end-to-end solution because they do not address the market dynamics once an antibiotic or diagnostic is licensed. The costs of R&D versus the return on investment and low probability of success² drive companies to move away from R&D. While diagnostic development costs are not as high as antibiotics, scientific challenges as well as the uncertainty of demand, use-cases and regulatory pathways result in poor incentives for innovation and access to diagnostics. Therefore, in the absence of a market that supports sustainable investment, pull incentives that incentivize R&D and access are needed. Complementary pull incentives that drive access, for example by LMICs, should also be considered.

RECOMMENDATION 4

National and regional regulatory bodies should adopt regulatory frameworks to facilitate development and regulatory approval of antibiotics as part of their efforts to achieve a regulatory system maturity commensurate with a stable, well-functioning and integrated regulatory system for medicines (WHO maturity level 3).

To unlock the full potential of the multi-billion-dollar investments required in R&D and to assure access to existing antibiotics and diagnostics, regulatory frameworks need to enable efficient clinical trials, product review and approval, and should be aligned with Good Regulatory Practices.³ While robust regulatory processes are essential, the complexity and cost of navigating separate submissions in each country can limit timely product availability. Regulatory authorities should apply regulatory reliance⁴ and ensure system maturity over the entire product life cycle, including testing, vigilance and postmarket surveillance.

RECOMMENDATION 5

National governments, WHO, partners, and donors should significantly expand efforts to increase access to essential antibiotics while ensuring their appropriate use.

The access challenges for both existing and newly available products are distinct and formidable. For existing products, issues such as global shortages, weak forecasting, insufficient financing or return on investment, inappropriate use, substandard and falsified products, and fragile supply chains persist, especially in LMICs. When point-of-care, rapid diagnostics do exist, there are significant accessibility and affordability barriers. Laboratory-based diagnostics are also a challenge given the costs of reagents, limited laboratory technicians, and challenging logistics. It can take years before LMICs have access to successful diagnostic and antibiotic innovations. National and supranational strategies, financing and greater concerted effort are needed.

RECOMMENDATION 6

Strengthen global coordination across the R&D and access continuum, building on existing fora and partnerships.

Collective action across the R&D and access value chain is needed to address the antibiotic crisis. This could include a pull incentive coordination 'hub' (e.g., enabled by the Global AMR R&D Hub) to align individual pull incentives, harmonize requirements for product inclusion and size, track progress, and assess effectiveness. It could also include a supranational mechanism (e.g., [SECURE](#)) to support LMICs with access to antibiotics and diagnostics. The current ecosystem benefits from positive collaboration, which should be strengthened to include a shared agenda, an end-to-end strategic orientation, and oversight of progress, gaps, risks, opportunities, and public health needs.

The GLG recognizes the need for R&D and access solutions across the One Health spectrum. A future and complementary piece of work, providing an in-depth analysis and prioritisation, should be carried out.

² The success rate from clinical phase 1 to commercialization is 12% (BCG, 2022). Of the 18 antibacterials launched since 2017, 17 have been placed on the Reserve list -- resulting in long lead-times (724 days on avg.) and/or withdrawals from regulatory approval. 10-year estimates of revenues might amount to only 40% of R&D and Commercialization costs. (EvaluatePhara, BCG 2022)

³ World Health Organization (2021). WHO Expert Committee on Specifications for Pharmaceutical Preparations. 55th Report. [link](#)

⁴ The act whereby a regulatory authority in one jurisdiction takes into account and gives significant weight to assessments by another regulatory authority or trusted institution or to any other authoritative information in reaching its own decision.

Background

At its sixth meeting in February 2023, the Global Leaders Group (GLG) on Antimicrobial Resistance (AMR) received a number of technical briefings and held an in-depth discussion on how the world is entangled in an antibiotic pipeline and access crisis. This is delineated by the diminishing effectiveness of current antibiotics, limited global access to antibiotics (novel and generic), and an insufficiency in the R&D pipeline for innovative antibiotics needed to treat drug-resistant infections. The lack of access to existing and innovative antibiotics is a contributor to the inappropriate use of antibiotics and the development of antimicrobial resistance. The GLG believes that antibiotics should be considered as global public goods, which should galvanize collective action to address the antibiotic pipeline and access crisis. While new R&D and access incentives are being piloted and implemented, they are still in their infancy and have yet to meaningfully impact global access and innovation.

The GLG is making six recommendations to address the antibiotic pipeline and access crisis. It has identified a set of solutions that can serve as the basis for advocacy and action in advance of the UN High-level Meeting on AMR in September 2024, help transform the recent G20⁵ and G7⁶ commitments around R&D and access into action, and catalyze global collective action.

Approach

These recommendations are based on interviews with GLG members and additional experts and stakeholders. Interviewees were asked for their insights and perspectives on priority solutions to the antibiotic pipeline and access crisis, including financial and non-financial solutions, means of collaboration across the R&D-to-access value chain, and potential barriers to the implementation of the solutions proposed. A literature review of more than 65 references was also conducted.

Scope

The primary focus of this report is on antibiotics⁷ for human use, but it is acknowledged that similar issues are occurring in other sectors, including animal health. Diagnostics have also gained prominence given their importance to stewardship and clinical care and the significant gaps in available products and access.

As AMR is not just a human health problem, but also an issue affecting the animal, plant and environment sectors, this report provides some illustration of linkages and potential solutions across the One Health spectrum. As reported by the Global AMR R&D Hub, less than 10% of total investments in R&D for AMR are in animal health. The GLG recognizes the need to look at R&D and access solutions across the One Health spectrum, and this report offers preliminary ideas, but does not provide an in-depth analysis. This should be prioritized in a future and complementary piece of work, including of a potential financial ecosystem to foster R&D priorities in the animal, plant and environment sectors.

These recommendations should be seen as part of comprehensive AMR action that includes prevention, surveillance, stewardship, evidence-generation efforts on the burden of AMR-related disease, and a clear economic case for investment, as well as a movement comprised of all facets of society, activated and nurtured by the sharing of evidence, information, and human-centered storytelling that drives political will. R&D and access to antibiotics have key dependencies with these topics, but these recommendations do not cover them in depth.

5 At its Health Ministers Meeting in India on 18-19 August 2023, the G20 “welcome[d] research and development on novel antimicrobials through various international initiatives such as SECURE, CARB-X & GARDP including push & pull mechanisms” The G20 expressed “continued support to the work of the Global AMR R&D Hub in promoting collaboration and coordination of R&D on AMR” and underlined “the importance of allocating funds to implement AMR National Action Plans (NAPs) from domestic mechanisms and relevant modalities of global financial instruments like the Global Fund, Pandemic Fund and AMR-specific mechanisms, such as the Quadripartite AMR Multi partner Trust Fund.”

6 On 13-15 May 2023, at the G7 Health Ministers meeting in Japan reiterated “the importance of a sustainable market for existing as well as new antimicrobials that promotes equitable access and stewardship and recognize[d] that there should be sufficient incentives in place to ensure such a market to meet public health needs. To this end, [they continued] to commit to exploring and implementing push and pull incentives that promote investment in R&D of antimicrobials, including contributing to existing global pooled efforts, such as CARB-X, GARDP and SECURE, at the earliest opportunity and within reasonable and feasible timelines.”

7 There is recognition that some of the challenges apply to other antimicrobials such as antifungals, etc. As they each have their own characteristics, the focus of these recommendations is on antibiotics.

Introduction and Context

As more antibiotics are used, the less effective they become due to the emergence and spread of drug resistance, necessitating perpetual innovation to outpace the natural evolution of bacterial species. There have been too few new antibiotics developed in the last few decades to keep pace with this evolution, as most new antibiotics build on existing mechanisms of action instead of new mechanisms with higher barriers to the development of resistance, rendering them susceptible to resistance and/or cross-resistance. Levels of resistance have risen and spread more rapidly than our ability to deliver new antibiotics. Large pharmaceutical firms have predominantly retreated from antibiotic R&D, citing the high risk of failure and a lack of sustainable return on investment, partly due to the classification⁸ and use of new products as ‘last- resort’ options (in order to increase the lifespan and effectiveness of new antibiotics and prevent rapid resistance development) which results in a low volumes and market size. Small and medium-sized enterprises (SMEs), which now drive most antibiotic R&D, face difficulty securing funding for preclinical and early clinical trials, and even more so for the costly late-stage R&D and post-marketing commitment, and they risk significant economic losses when commercializing. Increasing antibiotic resistance and lack a robust pipeline of new and innovative antibiotics have contributed to a global R&D crisis.

At the same time, many antibiotics - including quality-assured generics - can be inaccessible due to a range of issues including a lack of financing, poor demand quantification, supply-chain issues, proliferation of substandard and falsified medicines, and global shortages due in part to the lack of resilience in manufacturing, market exits triggered by diminished profitability, and a “race for the lowest price” by buyers. A challenge for all countries - but particularly in low- and middle-income countries (LMICs) and small countries - is that new antibiotics often remain inaccessible due to exclusive launches in larger markets and high-income countries (HICs). This is due in part to the complexity, cost, and time involved in registering new antibiotics across countries. This combination of factors results in an antibiotic access quandary, namely that excessive use of antibiotics coexists with a lack of access, accelerating the development and spread of resistance.

In addition, there is a critical gap of rapid, affordable, and decentralized diagnostics to reduce the misuse of antibiotics and combat AMR.⁹ Rapid diagnostics are needed for both pathogen identification and resistance testing. Innovations in biosensor techniques, optics, microfluidics, hybridization technologies and DNA amplification technologies have yielded new approaches. Unfortunately, these have not translated to meeting practical public health needs, such as molecular and point-of-care testing. Moreover, access to laboratory-based diagnostics is also a challenge due to the lack of a well-established laboratory infrastructure and skilled technicians in many settings, long turnaround times for results, and affordability barriers. Overall, the cost of diagnostic testing - which is often higher than the cost of antibiotic treatment and can substantially increase the total cost of care - is a significant barrier to the appropriate use of both diagnostics and antibiotics.

Strategic investment in new therapeutic options and diagnostics to combat AMR is imperative to address the unmet needs of patients, and to offset the exponentially increasing financial burden on global health systems.¹⁰ The cost of developing a new antibiotic is between US\$ 1.3-4.1 billion, while the expected revenue is US\$ 500 million throughout the patent period. Additional financing needed for early-stage product development is estimated to be US\$ 250 - 410 million per year,¹¹ and for late-stage development, the estimate is US\$ 310 million per year.¹² Although financing for R&D is beginning to increase, it remains vastly insufficient.¹³ The crisis requires more funding and long-term, even multi-decade, predictable funding to incentivize innovation, sustained action, and results. While the modelled return on investment for investing in antibiotic R&D with a global pull incentive value of US\$ 4.5 billion per antibiotic is high at 27:1 over 10 years and 125:1 over 30 years¹⁴ there is no certainty that funding will be available.

These financing needs are happening amid a global reflection on a new financial system that is fairer and more solidarity-based to meet shared global challenges: the fight against poverty, climate change and the promotion of diversity. The Bridgetown Initiative, the V20 Marrakesh Agenda, and the Summit for a New Global Financing Pact are identifying proposals to alleviate growing debt in climate vulnerable countries; change the terms of how funding is loaned and repaid; identify lending mechanisms for climate mitigation and resilience; and mobilize additional financing from the private sector. Some institutions/mechanisms are enhancing their support to AMR through their AMR-related or adjacent programs (Global Fund COVID-19 Response Mechanism (C19RM)), but this remains limited, and no major donors are present in the antibiotic access space. In the context of National Action Plans (NAPs) for AMR being substantially under- funded (i.e., 2023 reporting indicates fewer than 20% of NAPs are fully funded),¹⁵ this presents a further risk.

8 World Health Organization (2023). AWARe classification of antibiotics for evaluation and monitoring of use. [Link](#)

9 World Health Organization (2020). Lack of new antibiotics threatens global efforts to contain drug-resistant infections. [Link](#)

10 OECD (2015). Antimicrobial Resistance in G7 Countries and Beyond Economic Issues, Policies and Options for Action. [Link](#)

11 European Commission, European Health and Digital Executive Agency (2023). Study on bringing AMR medical countermeasures to the market – Final report. [Link](#)

12 Outtersson (2021). Estimating The Appropriate Size Of Global Pull Incentives For Antibacterial Medicines. *Health Affairs* 40:11. [Link](#)

13 Global AMR R&D Hub dashboard (October 2023). [Link](#)

14 Center for Global Development (2022). Estimating the EU's Return on Investment from an Ambitious Program to Incentivize New Antibiotics. [Link](#)

15 WHO-WOAH-FAO-UNEP (2023). Global Database for Tracking Antimicrobial Resistance (AMR) Country Self- Assessment Survey (TrACSS). [Link](#)

Funding alone is not enough to overcome the different barriers to R&D and access. Stimulating antibiotic R&D and safeguarding access to antibiotics demand a cooperative, multi-entity approach, blending the capacities of public and private sectors to maneuver through the challenges and construct resilient, equitable and sustainable access to antibiotics globally.

The GLG is making six recommendations for global action across a range of mutually reinforcing financial and nonfinancial solutions.

1 Establish shared global R&D targets with implementation roadmaps and target product profiles (TPP)

Challenges/issues:

The current approach to R&D is not resulting in a sufficient number or type of innovations. The absence of clear and shared R&D targets could scatter resources and efforts needed to tackle R&D priorities and deliver novel antibiotics. There is a risk that in the absence of goals and roadmaps, best efforts will inadvertently not target public health priorities and the global burden of disease, and that resources may not be mobilized due to a lack of overarching strategy. There is also a need for more precise and rapid diagnostic methods to identify infections accurately and facilitate timely and appropriate use of antibiotics in both human and animal health.

Context:

R&D for novel antibiotics has plummeted by 81% in recent years,¹⁶ presenting a dismal current pipeline.¹⁷ A widespread call for enhanced antibiotic R&D echoes across organizations, though specificity of targets remain elusive. Current efforts to map R&D investments (e.g., the Global AMR R&D Hub Dynamic Dashboard)¹⁸ is a good start, but proactive alignment on the size of the financial need and the set of incentives and actions needed should optimize funding and the likelihood of success. Well-defined targets – particularly if linked to appropriate financial incentives – could anchor a wider ecosystem, directing research, development and manufacturing, and facilitating funding and collaborative action. Global targets should not stifle regional or national priorities and pipelines, but bring focus to global priorities and risks, including longer-term and emerging needs. R&D targets that are translated into target product profiles (TPPs) have proven to be important signals and guides to the development of new products.¹⁹ Specification of techniques (like genome mining and new mechanisms of action) and desired characteristics (such as novelty, lower toxicity, and reduced treatment duration) are important signals to include in TPPs. Research roadmaps provide a strategic plan to achieve the target. Defining the portfolio of financial incentives needed to achieve the target will be a critical part of any roadmap. Increased coordination of R&D investments will help prioritize the highest potential societal impact and prevent overlap. Moreover, roadmaps that include measures to improve the overall robustness of the pipeline given the scientific challenges, stimulating greater interest in AMR as a field of study and research – in the way that climate has become a prestigious area of study – is also important,²⁰ as is supporting a diverse research base. There is also increasing recognition that greater attention to diagnostic R&D is needed. Among the diagnostics needed are rapid tests that distinguish between bacterial and viral infections, tests for pathogen identification, and tests for antimicrobial susceptibility patterns.

R&D priorities identified for the animal sector include 1) enhanced development of vaccines and deployment of vaccination programs, as they significantly contribute to improve animal health and reduce the overall need for antibiotics; 2) development and deployment of novel alternatives to antibiotics; and 3) more precise and rapid diagnostic methods to identify animal infections accurately and facilitate timely and appropriate use of antibiotics. Reference is made to STAR-IDAZ²¹ and its prioritization research roadmap,²² and to WOA reports prioritizing diseases where vaccines could reduce antimicrobial use.²³

16 Luepke (2017). *Past, Present, and Future Antibacterial Economics: Increasing Bacterial Resistance, Limited Antibiotics Pipeline, and Societal Implications*. [Link](#)
In: Center for Global Development (2023). *A New Grand Bargain to Improve the Antimicrobial Market for Human Health*. [Link](#)

17 World Health Organization (2022). *Antibacterial agents in clinical and preclinical development: an overview and analysis*. [Link](#)

18 [Global AMR R&D Hub Dynamic Dashboard \(globalamrhub.org\)](#)

19 World Health Organization (2023). *Strengthening health emergency prevention, preparedness, response and resilience*, p. 25. [Link](#)

20 O'Neil (2016). *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. [Link](#)

21 STAR-IDAZ International Research Consortium on Animal Health. *Coordinating animal health research globally to accelerate delivery of disease control tools and strategies*. [Link](#)

22 STAR-IDAZ International Research Consortium on Animal Health. *Research Roadmap Development for Alternatives to Antibiotics*. [Link](#)

23 WOA. *Reports from Adhoc groups on AMR*. [Link](#)

RECOMMENDATION 1

Working with governments, industry and other key stakeholders, WHO should lead the establishment of global shared R&D targets for antibiotics and diagnostics for human health, with implementation roadmaps and TPPs.

How this can be achieved:

- WHO priority pathogens,²⁴ representing the majority of AMR-related deaths, can serve as the starting point for establishing priority R&D targets.
- Targets should be based on an understanding of the current pipeline and the projected longevity of existing medicines, and be set using transparent prioritization criteria. Particular attention should be given to innovation and ensuring that the needs/use-case(s) of LMICs are included. For diagnostics, particular attention should be given to molecular, syndromic/multiplex and POC tests that are appropriate for use in LMICs.
- Targets should cover the near- and long-term (e.g., the number of new products reaching the market by priority pathogen over a defined time period). The G7 Shared Principles for Antimicrobial Valuation can be cross-referenced in terms of scientific attributes and unmet clinical needs. Targets should be translated to TPPs to further guide R&D.
- Research implementation roadmaps that provide a strategic plan to achieve each target should also be established. Roadmaps should define a portfolio of (e.g., push and pull) incentives to achieve an R&D target and the estimated financing needed. Artificial intelligence can be leveraged to model portfolio success rates.
- Implementation roadmaps can include actions that:
 - Establish frameworks for open collaboration in basic research, including with animal health platforms;
 - Increase research on non-traditional agents and non-therapeutic interventions (such as probiotics, bacteriophages, and phytochemicals.)²⁵ targeting bacterial virulence factors;
 - Support diversified research across LMICs and a range of settings;
 - Bolster scientific interest, aptitude, capacity, and prestige in the antimicrobial drug discovery field, and attract talent. With political will, this can be achieved through financing of training programs, scholarships, publications, and awards to appeal to early career academics and doctoral students; and
 - Establish a learning agenda to determine the effectiveness of different incentives that are a part of the portfolio, especially pull incentives given their novelty and funding needs.
 - The pharmaceutical sector should share information and insights related to push and pull incentives and experience, thereby enhancing the global understanding of these dynamics.
- Agencies involved in clinical trial development and regulation should 1) develop appropriate methodologies and evidence requirements for evaluating novel antimicrobials; 2) evaluate clinical trial designs; and 3) establish collaborative platforms and standardized protocols to equitably scale clinical trials.

²⁴ World Health Organization (2017). Prioritization of pathogens to guide Discovery, Research and Development of new antibiotics for drug-resistant bacterial infections, including tuberculosis. [Link](#)

²⁵ Gupta R, Sharma S. (2022). Role of alternatives to antibiotics in mitigating the antimicrobial resistance crisis. Indian J Med Res. 2022 Sep; 156(3): 464–477. [Link](#)

2 Push incentives for antibiotics and diagnostics

Challenge/issue:

To achieve a sustainable flow of new antibiotic drug candidates into and through the clinical pipeline, drug discovery and clinical development need to be strengthened and expanded. It is estimated that there is less than US\$ 200 million per year in antibiotic push funding²⁶ and some studies estimate that an additional US\$ 250 – US\$ 400 million per year is needed.²⁷ Additional support for diagnostics development is also needed.

Context:

WHO reports that there are more than 200 antibacterial agents/programs in the preclinical stage.²⁸ However, with one third of development programmes being discontinued each year, few make it to clinical development. Of the 27 products in clinical development (Phase I-III) targeting WHO bacterial priority pathogens, only two are active against at least one “critical” Gram-negative bacteria and fulfill at least one of WHO’s innovation criteria (i.e. absence of cross-resistance, new chemical class, mode of action or target). A holistic incentive package²⁹ including push mechanisms is essential to bolster the R&D pipeline. Push incentives help de-risk investments and make them more attractive to later-stage investors. Several initiatives including CARB-X, the REPAIR Impact Fund, AMR Action Fund, GARDP, and FIND are fueling innovation of antibiotic and diagnostic development with financial, scientific, regulatory, and technical support to the early stages of discovery into preclinical and clinical trial phases. Their scope ranges from antibiotics (traditional small molecules) to biological agents to vaccines and diagnostics, and they target different stages of development. The diversity of these efforts fosters dynamism, increases investment in novel approaches and mechanisms of action, and reduces the chance of perpetuating investments that may lack value. Given the scientific challenges of research and the anticipated risks linked with potential market failures, a portfolio of push incentives oriented toward R&D targets and roadmaps is essential. To achieve globally equitable impact, funders increasingly require that push incentives include global equitable access strategies involving actions such as adopting differentiated pricing strategies, fostering voluntary licensing, and building manufacturing capacities so that the people most in need will benefit from timely access to products enabled by push incentives. Public sector incentives for R&D and commercialization will be crucial for sustained innovation of genuinely groundbreaking antibiotics. Development of diagnostics is also needed to improve appropriate treatment, decrease unnecessary use, and preserve novel antibiotics, but has not been sufficiently prioritized.

RECOMMENDATION 2

Public and private funders/donors should increase funding for push incentives that support the development of antibiotics and diagnostics.

How this can be achieved:

Public and private funders should:

- Align push incentives with R&D targets and roadmaps.
- Strengthen and diversify R&D efforts. This includes working with research networks in LMICs and financing mechanisms (e.g., the European and Developing Countries Clinical Trials Partnership).
- Ensure that push incentive contracts include strong global equitable access strategies reinforced by the funder and the recipient of the push incentive (e.g., grantees have an access strategy for LMICs and funders require a strong access strategy) and are a part of acquisition contracts in the case of successful R&D outcomes.
- Ensure that push incentives appropriately target the R&D ecosystem, particularly developers in LMICs.
- Increase funding of research on non-traditional agents and non-therapeutic interventions (such as probiotics, bacteriophages, and phytochemicals).³⁰

26 Anderson M, Panteli D, van Kessel R, Ljungqvist G, Colombo F, Mossialos E.(2023). Challenges and opportunities for incentivising antibiotic research and development in Europe. *Lancet Reg Health Eur.* 2023 Jul 26;33:100705. [Link](#)

27 European Commission, Health Emergency Preparedness and Response Authority (2022). Study on bringing AMR Medical Countermeasures to the Market. [Link](#)

28 World Health Organization (2022). 2021 Antibacterial agents in clinical and preclinical development: an overview and analysis. [Link](#)

29 Anderson, Panteli and Mossialos (2023). How can the EU support sustainable innovation and access to effective antibiotics?: Policy options for existing and new medicines. [Link](#)

30 Gupta R, Sharma S.(2022). Role of alternatives to antibiotics in mitigating the antimicrobial resistance crisis. *Indian J Med Res.* 2022 Sep; 156(3): 464–477. [Link](#)

3 Pull incentives for antibiotics and diagnostics

Challenge:

Push incentives alone for antibiotics do not provide an end-to-end solution because they do not address market dynamics once an antibiotic or diagnostic is licensed. The costs of R&D versus the return on investment and low probability of success³¹ drive companies to move away from antimicrobial research. In absence of a market that supports sustainable investment in antibiotic R&D, there is a growing consensus on the potential effectiveness of pull incentives to deliver both R&D and access. While diagnostic development costs are not as high as antibiotics, the uncertainty of demand, unclear use-case targets, unclear regulatory pathways, and scientific challenges result in poor incentives for innovation and access to diagnostics.

Context:

To achieve the R&D targets, a holistic incentive package³² is needed, including pull mechanisms that address the market's inability to deliver sufficient return on investment into R&D. Pull incentives reward the successful development and availability of a product by increasing or ensuring future revenues.³³ Several G7 members have launched or are considering pull incentives to support antibiotic R&D³⁴ including Canada, the European Union, the United Kingdom and the United States. Other similar models such as Japan and Sweden are designed with the objective of enabling national access to antibiotics.³⁵ Pull financing mechanisms such as revenue guarantees and subscription models can be used to incentivize R&D and secure access to new products (depending on the level of investment) and have the advantage of delinking revenue from sales, which supports stewardship and appropriate use. Pull incentives are also catalytic because public funding creates an incentive for the private sector to invest resources at risk to develop and bring novel antibiotics to market. Pull incentives are complementary to push incentives and are only made when antibiotics are successfully brought to market. The Global AMR R&D Hub led a comprehensive landscape analysis of pull incentives for AMR.³⁶ Individual countries' pull incentives need to aggregate in way that meets the total investment needed to incentivize R&D, which could be US\$ 1 -4.1 billion per antibiotic per decade. As establishing a single fund for global pull incentives is not considered a realistic solution given national obligations, national pricing and reimbursement systems and political considerations, supranational coordination will be critical to ensure that incentives are sufficient and that they achieve the desired impact. Learning assessments and openness to adjustments will also be important given that it is a new approach and to ensure good stewardship of funds and results. The ability to impact global access is also likely to depend on the size and nature of pull incentives. Provisions for global/LMIC access are largely absent from current mechanisms as identified by the Global AMR R&D Hub and WHO in their progress report for the G7.³⁷ Market entry reward-type pull incentives for diagnostics, such as the AMR Longitude Prize³⁸ and the U.S. National Institute of Health Antimicrobial Resistance Diagnostic Challenge,³⁹ are also being used to incentivize R&D and access, but to be successful they need a pipeline of diagnostic candidates and can take several years to materialize.

31 The success rate from clinical phase 1 to commercialization is 12% (BCG, 2022). Of the 18 antibacterials launched since 2017, 17 have been placed on the Reserve list -- resulting in long lead-times (724 days on ave.) and/or withdraws from regulatory approval. 10-year estimates of revenues might amount to only 40% of R&D and Commercialization costs. (EvaluatePhara, BCG 2022)

32 Anderson, Panteli and Mossialos (2023). How can the EU support sustainable innovation and access to effective antibiotics?: Policy options for existing and new medicines. [Link](#)

33 Examples of pull incentives are outlined in: Global AMR R&D Hub & Stakeholder Group, A shared dialogue on pull incentives (2023), [Link](#) and European Commission, Study on bringing AMR Medical Countermeasures to the Market (2022) [Link](#)

34 <https://amr.solutions/incentives/>

35 Global AMR R&D Hub & WHO (2023). Incentivising the development of new antibacterial treatments. Progress Report. [link](#)

36 Global AMR R&D Hub & Stakeholder Group (2023). A shared dialogue on pull incentives. [Link](#)

37 Global AMR R&D Hub & WHO (2023). Incentivising the development of new antibacterial treatments. Progress Report. [link](#)

38 <https://amr.longitudeprize.org/>

39 <https://dpcpsi.nih.gov/AMRChallenge>

RECOMMENDATION 3

The G7 and G20 should each play their role in establishing pull incentives to support R&D and enable access to antibiotics and diagnostics.

How this can be achieved:

- Building on the commitments and momentum created by the G7, the G7 and EU, with support from the G20, WHO, and other stakeholders including the private sector should lead on establishing pull incentives aligned with R&D targets and research roadmaps. The total target level for a global pull incentive for R&D (value and volumes) should be established, linking the size of a new product's incentive to its public health value (such as complying with a TPP). Fair sharing estimates of the cost should be established, drawing on example methodologies that recognize that the G7 and EU contribute significantly to pull incentives.⁴⁰
- The potential for an equitable access-focused mechanism targeting LMIC needs (e.g., revenue guarantee) should be explored. This should build on the access provisions of other push and pull incentives, (e.g., by working with generic companies that hold a voluntary license to produce a novel antibiotic from an innovative company that received pull incentives in HICs), and should support registration in LMICs and affordable pricing.
- Additional pull incentives for diagnostics should also be explored, such as a market entry rewards and/or advance market commitments (i.e. guaranteed procurement volumes).
- The G7 and G20 should establish a pull incentive “coordination” hub (e.g., enabled by the Global AMR R&D Hub) to help align individual pull incentives, harmonize requirements for product inclusion, sizing, tracking progress, and assessing effectiveness.
- In response to R&D targets and adequately sized pull incentives, developers and companies should increase their investment in antibiotics and diagnostic R&D.
- Pull incentive contracts between a government and manufacturer should include mutually agreed terms with appropriate levels of transparency (See example below, developed for these recommendations).^{41, 42}

Example of potential terms and commitments of pull incentives



Key terms of pull incentives:

- Provision of guarantee/reward to the manufacturer that is de-linked from volumes/sales
- Workable with/tailored to national systems and structures
- Preferably, incentivize both R&D and access
- Leverage strong global access and include stewardship provision



In exchange, manufacturers should commit to:

- Work with governments and other stakeholders to maintain sufficient (local-level) product availability
- Support and facilitate appropriate stewardship
- Apply (independent and recognized) manufacturing standards to limit environmental contamination
- Establish global access strategy/commitments, (e.g., such as voluntary licensing, equitable pricing strategies, manufacturing capacity building, etc.)
- Be transparent with key terms, and provide timely information when they foresee availability challenges/bottlenecks

40 Center for Global Development (2022), Estimating the EU's Return on Investment from an Ambitious Program to Incentivize New Antibiotics (2022). [Link](#) and BCG (2022). The Case for a Subscription Model to Tackle Antimicrobial Resistance. [Link](#)

41 AMR Industry Alliance (2022), Minimizing risk of developing antibiotic resistance and aquatic ecotoxicity in the environment resulting from the manufacturing of human antibiotics. [Link](#)

42 Global Leaders Group on AMR (2022). Reducing Antimicrobial Discharges from Food Systems, Manufacturing Facilities and Human Health Systems to the Environment. Call to Action by the Global Leaders Group on AMR. [Link](#)

4 Strengthen and streamline regulatory frameworks to facilitate development and regulatory approval of antibiotics

Challenge/issue:

To unlock the full potential of the multi-billion-dollar investments required in R&D for global benefit and to ensure access to existing antibiotics and diagnostics, regulatory frameworks need to enable timely trials, product review and approval, and should be aligned with Good Regulatory Practices. While robust regulatory processes are essential, the complexity and cost of navigating separate submissions in each country can limit timely product availability. Streamlining these processes and approaches is therefore a priority to help ensure access to new products.

Context:

Topics identified for potential regulatory streamlining include evidence requirements for novel antibiotics and diagnostics, clinical trial requirements across countries, and country-to-country product registration. Because regulatory systems can be resource intensive, regulatory reliance and regional regulatory collaboration are important to bring efficiencies by avoiding duplication and improving the allocation of resources. Regional regulatory collaboration and reliance are demonstrating improvements in efficiency and capabilities, and helping to ensure quality. Examples of successful regional approaches include the European Medicines Agency (EMA), The ASEAN Pharmaceutical Regulatory Policy,⁴³ the Caribbean Regulatory System⁴⁴ (CRS), the Southern African Development Community Medicines Regulatory Harmonization (SADC-MRH) initiative through the ZAZIBONA Collaborative Procedure, East African Community Medicines Regulatory Harmonization Programme (EAC-MRH), and African Vaccine Regulatory Forum (AVAREF). Collaborative regional approaches also promote diversified manufacturing, which has been identified as a potential solution to improving access.

RECOMMENDATION 4

National and regional regulatory bodies should adopt regulatory frameworks to facilitate development and regulatory approval of antibiotics as part of their efforts to achieve a regulatory system maturity commensurate with a stable, well-functioning and integrated regulatory system for medicines and diagnostics (WHO maturity level 3).

How this can be achieved:

- Streamline new product registration pathways including via reliance platforms.
- Perform evaluations of regulatory systems using the WHO Global Benchmarking Tool (GBT) to identify capacity gaps and elaborate through the institutional development plans (IDPs).
- Explore setting targets to achieve progress towards a stable, well-functioning and integrated regulatory system (WHO Maturity Level 3) for medicines and other health products. Doing so could also help direct national or donor-supported resources to strengthen regulatory systems.
- Implement regulatory harmonization, convergence and collaboration to facilitate the adoption of reliance pathways for accelerated regulatory approval of antibiotics.⁴⁵
- Incorporate the concept of reliance on national/regional regulatory policies, regulations and guidelines on work done by other advanced and trusted regulators and including through WHO's collaborative registration procedure (CRP).⁴⁶
- Apply reliance and ensure system maturity over the entire product life cycle, including assessment, testing, vigilance and post-marketing surveillance.
- Consider revising registration fees for certain products, particularly low-volume products for which incentives to register/supply may be lacking.
- Establish regulatory pathway and frameworks for diagnostics, considering the latest guidance from WHO, and particularly the [Global Benchmarking Tool + Medical Devices and In Vitro diagnostics](#) as well as the Global Model Regulatory Framework for Regulation of medical devices including in vitro diagnostic medical devices.⁴⁷

43 ASEAN Pharmaceutical Regulatory Policy, Adopted intersessionally by AEM on 15 March 2022 and AHMM on 15 June 2022 <https://asean.org/wp-content/uploads/2022/08/Final-Text-APRP-adopted-AEM-and-AHMM.pdf>

44 Caribbean Public Health System: <https://carpha.org/What-We-Do/CRS/Caribbean-Regulatory-System>

45 One Health Trust (2022). Drug Regulatory Approvals and Opportunities for Antimicrobial Innovation, Perspectives from Brazil, India and South Africa. [Link](#)

46 World Health Organization (2019). Delivering Quality Assured Medical Products for All, 2019-2023. [Link](#)

47 World Health Organization (2017). WHO Global Model Regulatory Framework for Medical Devices including in vitro diagnostic medical devices. [link](#)

5 Initiatives to improve access to antibiotics and diagnostics

Challenge/issue:

The access challenges for both existing and newly available products are distinct and formidable. For existing products, issues such as global shortages, weak forecasting, insufficient financing or return on investment, inappropriate use, and fragile supply chains persist, especially in LMICs. Shortages of amoxicillin have been reported in 80% of the 35 countries for which WHO had data⁴⁸ But the access situation is global: in January 2023, the European Medicines Agency reported amoxicillin shortages in 24 Member States.⁴⁹ In the United States, antibiotics accounted 10% of medicine shortages in 2022.⁵⁰ For new products that are considered innovative, typically classified as “Reserve”, low volumes mean that a viable market is absent, and developers/manufacturers often do not register their products in small countries and/or LMICs. Only 12 of the 25 new antibiotics that entered the market between 1999 and 2014 were registered in more than ten countries.⁵¹ When point-of-care, rapid diagnostics exist, they are often not widely available due to accessibility and affordability barriers. Laboratory-based diagnostics are also a challenge given the laboratory structure and testing capabilities needed at each level of the public healthcare system, limited laboratory technicians, and challenging and time-consuming logistics. It can take years before LMICs have access to successful diagnostic and antibiotic innovations and before global equitable access is realized.

Context:

Many of these access challenges would benefit from national strategies, such as moving to multi-year procurement contracts for antibiotics; national capabilities, such as strategic stockpiling, improved forecasting; and supranational collaboration, such as guidelines for simplifying antibiotic portfolios and pooled procurement or procurement consortiums. Currently there is limited donor attention to improving access to antibiotics and diagnostics coherency in LMICs, which can make global action more difficult. However, some organizations are starting to consider antibiotics as a complementary programming area, such as support by the Global Fund to Fight AIDS, TB and Malaria for co-infections and co-morbidities.⁵²

48 Mancini, Kuchler (2022). Infection growth stokes global lack of antibiotics. [link](#)

49 European Medicines Agency. Shortages of amoxicillin and amoxicillin/clavulanic acid. 27 January 2023. EMA/27040/2023 Rev1. [link](#)

50 US Pharmacopeia Medicine Supply Map, May 2022. [Link](#)

51 Introduction and geographic availability of new antibiotics approved between 1999 and 2014 (2018), [Link](#)

52 The Global Fund (2015). Thirty-Third Board Meeting Global Fund support for coinfections and co-morbidities GF/B33/11 [Link](#)

RECOMMENDATION 5

National governments, WHO, partners, and donors should significantly expand efforts to increase access to essential antibiotics and diagnostics while ensuring their appropriate use.

How this can be achieved:

National governments should further improve access based on their situation:

- Ensure that antibiotics and diagnostics plans are included in financially-supported NAPs for AMR and leverage funding opportunities such as the Pandemic Fund and the Global Fund.
- Mitigate antibiotic shortages, including by monitoring risks of market withdrawals and taking early action, and explore diversification of supply, such as through tenders that require multiple winners. Maintain current antibiotic production capacity and explore the potential for expansion including Active Pharmaceutical Ingredients (API).
- Strengthen antibiotic and diagnostic supply chains and improve manufacturing predictability, including appropriate strategic stockpiling, multi-year procurement and other contracting conditions, such as volume commitments and awards based on assuring supply rather than only lowest price, and as appropriate, work with supranational pooling/consortium mechanisms. Improve forecasting with better surveillance data, e.g., through point prevalence studies.
- Simplify antibiotic portfolios through prioritization, optimization, or harmonization to support clinical best practice and improve the efficiency of forecasting and procurement and supply.
- Target antibiotics to the right patients, in line with WHO's AWaRe (Access, Watch, Reserve) classification and [The WHO AWaRe antibiotic book](#), including through access to quality diagnosis, up-to-date, evidence-based treatment guidelines and implementation of antimicrobial stewardship strategies at national and facility levels. Implement action plans to meet the AWaRe stewardship target of 60% consumption within Access antibiotic class to improve stewardship.
- Develop and implement introduction strategies for new products exiting the pipeline, which are usually Reserve products needed to treat life-threatening drug resistant infections.

At supranational level:

- Empower initiatives (e.g., SECURE)⁵³ to support LMICs with capability and strategy that drive equitable access to both new and existing antibiotics and diagnostics. Specific interventions include product licensing, simplification of antibiotic portfolios, product launch strategies, forecasting pooled/coordinated procurement, and market intelligence. The G20 with WHO and other stakeholders should consider establishing a funding mechanism to systematically support this work.
- Take steps to ensure that antibiotic procurement drives supply security by diversifying manufacturing, including of API, with the aim of improving sustainable and global access to affordable, quality-assured antibiotics and achieving market equilibrium between demand and the number of manufacturers. The current plans to increase regional production platforms should take care not to fragment fragile antibiotic supply chains and achieve an appropriate balance between diagnostics, therapeutics and vaccines.
- Manufacturers and developers should implement global access strategies for their products, which could include actions such as adopting equitable pricing strategies, fostering voluntary licensing, and building manufacturing capacities.
- With the support of pull incentives and access mechanisms, manufacturers should strive to ensure sustainability of supply, transparency with regard to production challenges, and timely delivery of Reserve antibiotics.

⁵³ SECURE's mission is to expand access to essential antibiotics to support countries in addressing the silent pandemic of drug-resistant bacterial infections. Through this initiative, participating countries will have access to essential new antibiotics designed to address drug-resistant infections, alongside essential older antibiotics not widely available or subject to frequent supply chain disruptions. <https://www.who.int/groups/secure-expanding-sustainable-access-to-antibiotics>

6 Reduce fragmentation and achieve results by coordinated action

Challenge/issue:

Collective action across the R&D and access value chain is needed to address the antibiotic pipeline and access crisis. Although the current ecosystem benefits from positive collaboration, notably via the Global AMR R&D Hub, it is fragmented and lacks a shared agenda, an end-to-end strategic orientation, and oversight of progress, gaps, risks, opportunities and public health needs. Moreover, there is no means of monitoring national and supranational action, including to provide transparency on the broader AMR actions and obligations from which the R&D and access work could benefit.

Context:

Several areas requiring alignment and coordination to achieve impact have been identified. While numerous global and regional actors/partners are focusing on upstream R&D, far fewer are working on antibiotic access. The Global AMR R&D Hub serves as one conduit for information exchange in the upstream, and SECURE is emerging as one mechanism focused on improving access to both new and existing antibiotics. The global and local pharmaceutical industry and other private sector actors possess a wealth of expertise, capability, and assets, and play a pivotal role in addressing the crisis as part of the collective action needed.

RECOMMENDATION 6

Strengthen global coordination across the R&D and access continuum, building on existing fora and partnerships.

How this can be achieved:

- Ensure overall monitoring of progress on the R&D targets and roadmaps (e.g., through WHO)
- R&D / pipeline coordination: Monitor R&D and early market access financial needs, allocations, and gaps. Encourage collaboration, cooperation, and transparency on key activities, and identify a platform for exchange of best practices and learnings (e.g., through the Global AMR R&D Hub and/or regional entities such as the Health Emergency Preparedness and Response Authority (HERA)).
- Pull Incentive Hub: Establish a means for alignment on pull incentives – sizing, stacking, tracking, and assessing effectiveness (e.g., G7 and G20 countries with a rotating chair, supported by the Global AMR R&D Hub).
- Access coordination and LMIC support (e.g., SECURE and G20 countries): Demand estimation, pooled/coordinated procurement, intercountry strategic stockpiling strategies, guidance on new antibiotic uptake, exchange of lessons from pooling strategies (such as those being explored by European Union).
- National governments should explore an accountability mechanism for AMR, from which R&D and access would benefit (e.g., commit to tackling AMR as a part of the INB negotiation outcome; consider an international instrument).
- Pioneer long-term financing solutions for R&D and access financing needs, in addition to AMR NAP financing (e.g., engaging the emerging Global Financing Pact, including the Bridgetown Initiative).
- Development finance institutions, the Global Fund, the Pandemic Fund, the Coalition for Epidemic Preparedness Innovations (CEPI), Unitaaid and other existing sources of funding for public health goods should pay more attention and allocate more funding to antibiotic R&D and access.
- Establish a public-private collaborative platform for information exchange, monitoring, and strategic orientation.