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# Incentivising the development of new antibacterial treatments 2023

Progress Report by the Global AMR R&D  
Hub & WHO

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# AMR: A socio-economic crisis

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In 2021 and 2022, G7 Finance and Health Ministers committed to expedite implementation of existing antimicrobial resistance (AMR) strategies, to take additional steps to address antibiotic market failure, create economic conditions to preserve the effectiveness of essential existing antibiotics and ensure their access, strengthen AMR research and development (R&D), and bring novel antibacterials to market that address public health needs<sup>1,2,3</sup>. An [initial progress report](#) was prepared by the Global AMR R&D Hub and WHO for the G7 Finance and Health Ministers in May 2022, with a [progress update](#) requested for 2023. The present report is a response to this request providing an update on the financial landscape for developing new and innovative antibacterials, country-by-country progress on commitments and key areas for action in the next two years.

## Challenges & Opportunities

- **AMR remains one of the top 10 global public health threats facing humanity**, associated with the deaths of 4.95 million people in 2019, more than HIV or malaria. Notably, 1 in 5 of the deaths caused by AMR occurred in children under the age of five<sup>4</sup>. Across the G7, almost half a million lives could have been saved in 2019, if all drug-resistant infections were prevented<sup>5</sup>. In comparison with other diseases, although effects are felt across all life stages, they are inherently reversible with a usually short course of treatment returning individuals to a productive and healthy life.
- **AMR is a threat to the global economy, with impacts on international trade, health care costs and productivity**. If no action is taken, AMR could cost the world's economy USD 100 trillion by 2050<sup>6</sup>. The World Bank<sup>7</sup> predict losses of up to 3.8% of gross domestic product (GDP) globally by 2050, throwing an estimated 28 million people into poverty and increases in health care costs estimated in the range of 1 trillion USD per year by 2030 (In high income countries, this equates to an estimated 6% increase in annual health care costs<sup>8</sup>). The Quadripartite organisations are currently assessing the broader economic impact of AMR across sectors in the short term and results will be available in due course.
- **Antimicrobials - and antibiotics in particular - are key infrastructure for health systems**, and the cornerstone of modern healthcare, but the R&D [pipeline for new antibacterials is "insufficient"](#)<sup>9</sup> to tackle the challenge of increasing emergence and spread of antibiotic resistance. According to WHO, only 77 new antibacterial treatments are in clinical development<sup>10</sup> and most are derivatives of existing antibiotic classes with well-established mechanisms of drug resistance, and the majority are unlikely to make it to market<sup>11</sup>. Furthermore, the [Global Leaders Group on AMR](#) reiterated that the world faces a serious antibiotic pipeline and access crisis that requires innovative financing measures.

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<sup>1</sup> G7 Finance Ministers' Statement on Actions to Support Antibiotic Development, 13 Dec. 2021, UK [accessed 9th March 2023]

<sup>2</sup> G7 Health Ministers' Communiqué 20 May 2022, Berlin [accessed 9th March 2023]

<sup>3</sup> G7 Finance Ministers and Central Bank Governors' Petersberg Communiqué, 20 May 2022 [accessed 9th March 2023]

<sup>4</sup> Murray et al. 2022 Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis - The Lancet [accessed 1st March 2023]

<sup>5</sup> The Burden of Antimicrobial Resistance in G7 Countries and Globally: AN URGENT CALL FOR ACTION [accessed 1st March 2023]

<sup>6</sup> Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. The Review on Antimicrobial Resistance Chaired by Jim O'Neill December 2014 [accessed 1st March 2023]

<sup>7</sup> Jonas et al. 2017 Drug-resistant infections: a threat to our economic future: executive summary (English). HNP/Agriculture Global Antimicrobial Resistance Initiative Washington, D.C.: World Bank Group. [accessed 1st March 2023]

<sup>8</sup> European Observatory on Health Systems and Policies (2019). Averting the AMR crisis: What are the avenues for policy action for countries in Europe? [accessed 10th April 2023]

<sup>9</sup> <https://www.who.int/news/item/22-06-2022-22-06-2022-lack-of-innovation-set-to-undermine-antibiotic-performance-and-health-gains> [accessed 31st March 2023]

<sup>10</sup> Clinical development comprises phase 1-3 clinical trials to New Drug Applications (NDA)

<sup>11</sup> <https://wellcome.org/news/drug-resistant-infections-science-economics> [accessed 31st March 2023]

- **There is no viable market for novel antibiotics.** The return on investment for new ‘reserve’ antibiotics fails to cover the costs of their development, manufacturing and distribution<sup>12</sup>. As a result, major pharmaceutical companies have backed away from antibiotic development, and the enterprises, often small or micro biotech, remaining in the space struggle to sustain their operations.
- **Availability and access to new and existing antibiotics, including generics, across many G7 countries and beyond can be unreliable<sup>13</sup>,** increasing the socio-economic impacts of AMR.
- **Push incentives** - government or regulatory interventions which support R&D by directly lowering the costs of development - have contributed to mitigating some of the challenges associated with antibacterial development, but in isolation and at the current scale, are insufficient to meet R&D objectives and bring sufficient products to market. In addition, mechanisms for equitable and appropriate access once products are developed are limited. Without a viable market, industry representatives have signaled investment in AMR R&D will continue to decrease<sup>14</sup>.
- **Policies rewarding R&D programs that successfully bring products to market and ensure access** (see [Box 1](#)) - **pull incentives** (see [Annex 1](#)) **or other innovative financing mechanisms** - will help support the development of a sustainable pipeline of novel antibacterials and reinvigorate innovation across the life sciences ecosystem, with positive impacts across the G7 on health, productivity and economic growth.
- **Ensuring a sustainable supply of existing and novel antibacterials to address public health needs globally is a central component of securing a resilient, safe, and economically productive future.**

#### Box 1: Ensuring access to priority antibiotics

The [Global AMR R&D Hub’s studies](#) highlight a worsening access gap, whereby effective antibiotics are not available in the parts of the world at scale, where the need is most dominant and growing most rapidly. With need spread unevenly across many national markets, access is precarious in low- and middle-income countries (LMICs), but also in some high-income countries (HICs). There is therefore the need for cooperation and further engagement across countries, donor agencies and public-private partners to ensure equitable access to priority antibiotics and diagnostics for those with the greatest need.

## The current financial landscape for sustainable AMR R&D

- **Since 2022, G7 countries have been engaging in a range of activities to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market,** underpinned by the [2021 G7 Shared Principles for the Valuation of Antimicrobial Therapeutics](#). The United Kingdom (UK) is considering scaling up its existing subscription model for new antibiotics. Japan, Canada, the European Union (EU) and United States of America (US) are all at various stages of evaluating and implementing economic models for encouraging market entry and sustained market availability of high-value antimicrobials, with Japan recently announcing a revenue guarantee program for novel antibiotics which will start in 2023. Germany has proposed new revised pricing and reimbursement laws for reserve antibiotics ([ALBVVG](#)) against multi-drug resistant bacteria and [pledged a further EUR 50 million for GARDP](#), the US committed up to [USD 300 million for CARB-X](#), while Canada pledged financial support for [SECURE](#) (see [Box 2](#)). France published its national strategy for preventing infections and antibiotic

<sup>12</sup> Global AMR R&D Hub, 2021. Estimating global patient needs and market potential for priority health technologies addressing antimicrobial resistance. [accessed 31st March 2023]

<sup>13</sup> Otterson et al. 2022. Clin Infect Dis. 74(7):1183-1190. doi: 10.1093/cid/ciab612.

<sup>14</sup> AMR Industry Alliance, February 2022. Progress Report: AMR Industry Alliance 2021 Survey. [accessed 9<sup>th</sup> March 2023]

resistance, which includes promoting innovative R&D and the French HTA authority (HAS) issued its new [principles of evaluation of the Transparency Commission relating to drugs with respect to their access to reimbursement](#). Italy has published a [report on antibiotic use, covering expenditure for antibiotics](#) and its second National Action Plan on AMR 2022-2025. See [Table 1](#) for a detailed overview of country-by-country progress across the push and pull continuum and [Table 2](#) for a summary of the key features of existing and proposed pull incentives.

- **Investments in AMR R&D from public and philanthropic sources globally equate to USD ~1.6 – 1.8 billion per year<sup>15</sup>.** Since 2017, public and philanthropic investments in AMR R&D globally across all One Health sectors have reached USD 10.67 billion – an increase of over USD 1.67 billion since April 2022.
- **The G7 + EU continue to lead AMR R&D financing across the One Health spectrum<sup>16</sup>.** This includes investments in the development of health technologies addressing AMR, such as therapeutics, diagnostics and vaccines. In addition, G7 countries continue to invest in relevant partnerships to accelerate the development and market entry of needed new antimicrobials (e.g., through [CARB-X](#), [GARDP](#), [Innovative Medicines Initiative](#), [InnovFin Infectious Diseases](#)). Contributions to CARB-X and GARDP alone are dominated by G7 countries (99% of total contributions, USD 939 million), with the US, UK and Germany, providing the highest financial contributions (98% of total funding volume to date)<sup>16</sup>. In May 2022, the US committed up to [USD 300 million \(plus USD 70 million from Wellcome Trust\) over 10 years for CARB-X](#), and in October 2022, [Germany pledged EUR 50 million in further support for GARDP \(2023-2027\)](#).
- **Private sector contributions to AMR R&D are claimed to be ~1.8 bn USD annually<sup>17</sup>,** but due to the lack of return on investment (ROI) for antibiotics R&D in particular, more profitable areas, such as oncology are favored<sup>18</sup>. The [AMR Action Fund](#), which was established by a coalition of pharmaceutical companies with the support of WHO, the European Investment Bank and Wellcome Trust to bring 2-4 new antibiotics to patients by 2030, made its first two investments in April 2022 and has extended its portfolio with investments in companies developing traditional antibiotic therapies, non-traditional phage-based therapies and a diagnostics platform for rapid pathogen testing.
- **The small biotech companies and research groups developing the most promising pre-clinical antibacterial R&D projects need additional push funding to replenish a weak clinical pipeline.** An analysis based on data from the Global AMR R&D Hub's [Dynamic Dashboard](#) plus other sources estimated how much funding and investments can be expected in the coming ten years for antibacterial R&D from private investors, G7 countries and the European Commission (EC), initiatives like CARB-X and the AMR Action Fund, plus others. It then compared this amount to what would be needed to sustain a pipeline delivering at least six 'high impact' antibiotics over the next decade<sup>19</sup>. The preliminary results draw renewed attention to a significant funding gap in the pre-clinical stages of R&D. This is particularly worrying because, as highlighted by WHO<sup>9</sup>, the pre-clinical pipeline is where the most promising and innovative R&D projects are. Yet, these projects are often led by financially vulnerable product developers (mostly small or even micro biotech companies). Accelerating the most promising R&D projects in pre-clinical development will provide much needed replenishment of a weak clinical pipeline.
- **The G7 could potentially benefit both economically and socially from investing in an antibiotic pull incentive program addressing the most urgent public health needs.** Recent work from the

<sup>15</sup> Values based on data from the Global AMR R&D Hub's Dynamic Dashboard (>13,000 AMR R&D projects)

<sup>16</sup> At the current time it is not possible to provide an accurate comparison of yearly investments on a country-by-country basis for the period 2022-2023, using the Global AMR R&D Hub's Dynamic Dashboard data. This data will be available in the very near future.

<sup>17</sup> AMR Industry Alliance, February 2022. Progress Report: AMR Industry Alliance 2021 Survey. [accessed 9<sup>th</sup> March 2023]

<sup>18</sup> Thomas D, CFA & Wessel C. BIO Industry Analysis, 2022. The State of Innovation in Antibacterial Therapeutics. [accessed March 9<sup>th</sup> 2023]- report highlights that there has been 17 x more funding for oncology companies as compared to antibacterial investment over the last decade (USD 26.5 bn vs USD 1.6 bn – US only).

<sup>19</sup> Estimate based on range reported in the following publications: ISDA 10 x 20 initiative; Review on Antimicrobial Resistance 2016; Breaking through the Wall, 2017; DRIVE-AB, 2018; <https://aspe.hhs.gov/reports/national-action-plan-combating-antibiotic-resistant-bacteria-2020-2025>; BARDA strategic Plan 2022-2026

[Centre for Global Development](#) (Silverman & Towse 2022)<sup>20,21</sup> has evaluated the benefits and costs to the G7 and EU of a new antibiotic incentive program, which would seek to generate a total of 18 new antibiotics over three decades to treat six priority pathogens (i.e. 6 per decade). Other reports proposing ‘fair share’ contributions to antibiotic development are also available – see also *Boularte & Schultze 2022*<sup>22</sup> and *Brassel et al, 2023*<sup>23</sup> for further discussion of this topic.

## Next Steps & Key Action Areas for G7 countries

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Building on the progress across the G7 over the last year, the following next steps for priority actions for Finance and Health Ministers are recommended with an outlook to deliver concrete action over the next two years:

### Renew Priorities and Timelines

Addressing AMR and its socio-economic impacts is a priority for G7 countries and beyond requiring shared priorities and timelines for action.

Recommendations:

- Further recognize and commit to tackle AMR within international political discussions and accords on pandemic preparedness and response.
- Work towards tangible and specific commitments and targets for G7 action on incentivizing the development of and equitable access to new antibacterials for agreement in the next two years, including contributing towards specific commitments and targets at the high-level meeting on AMR at the United Nations General Assembly in 2024.

### Encourage Alignment and Targeted Action on Financing Mechanisms, including Push and Pull Incentives

Recognizing that push incentives on their own - at the current scale - are not sufficient to drive the development of new antibacterials beyond the R&D phase, concerted and ambitious actions are needed for the development and implementation of pull incentives or other innovative financing mechanisms.

Recommendations:

- Strengthen the AMR R&D ecosystem across the development pipeline through sustainable and predictable financing and resources to address the antibiotic R&D and access crisis, including commitment to further financing of public-private partnerships such as CARB-X and GARDP.
- Build on country-level experience gained through implementation and evaluation of pull incentive pilot approaches and explore the possibility of formulating international collaborative mechanisms on pull incentives for antibacterial R&D, as appropriate.
- Call on the Global AMR R&D Hub to establish a clear process for sharing information and evaluation of pull incentive models across countries, and to share recommendations with the G7 on coordination opportunities in 2024.
- Ensure pull mechanisms are designed to stimulate R&D and reward innovation, and provide appropriate global and equitable access, including for low- and middle-income countries that experience the highest burden of resistance.

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<sup>20</sup> Estimating the EU's Return on Investment from an Ambitious Program to Incentivize New Antibiotics (cgdev.org) [accessed 9<sup>th</sup> March 2023]

<sup>21</sup> G7 Investments in New Antibiotics Would Pay Off Big—For Everyone (cgdev.org) [accessed 9<sup>th</sup> March 2023]

<sup>22</sup> Boluarte T & Schulze U. BCG, 2022. The Case for a Subscription Model to Tackle Antimicrobial Resistance [accessed 10<sup>th</sup> March 2023]

<sup>23</sup> Brassel et al. 2023. Incentivising New Antibiotics: Designing a Value-Based Delinked Pull Incentive. OHE Contract Research Report, London: Office of Health Economics. [accessed 4<sup>th</sup> April 2023]

## Prioritize Equity and Global Access to Priority Antibacterials

Although the development of new and novel antibacterials should be prioritized, broadening equitable and global access to novel and existing antibacterials is also essential.

Recommendations:

- Strengthen and build on commitments from G7 countries to support initiatives to ensure and improve global and equitable access to new and existing antibiotics, such as [SECURE](#).
- Bolster equitable and global access to antibiotics addressing the most urgent public health needs, and other essential health products for AMR, including diagnostics and vaccines, e.g., through better integration of AMR into international development co-operation initiatives and inclusion of access provisions in relevant push funding agreements.

### Box 2: SECURE - Expanding Sustainable Access to Antibiotics

[SECURE](#) is being developed by the World Health Organization (WHO) and the Global Antibiotic Research and Development Partnership (GARDP) with input from the United Nations Children’s Fund (UNICEF) and the Clinton Health Access Initiative (CHAI). SECURE will improve access to essential antibiotics while investing in stewardship and help generate data on local AMR conditions and the effective use of newly approved antibiotics. It has the potential to bring about new procurement and supply financing models and will provide a desperately needed pull for more investment in antibiotic development. SECURE’s antibiotic portfolio will be adapted to countries’ individual needs, including both generic antibiotics that are in short supply or are not widely available, and newly approved Reserve antibiotics to treat resistant bacterial infections.

**To maintain momentum, the Global AMR R&D Hub and WHO could – if considered useful – provide a further progress update under Italy’s G7 Presidency in 2024**

AMR is a truly global problem, requiring a multifaceted, coordinated and collaborative approach across countries, including target setting and agreement on burden sharing for the development of new antibacterials (and other technologies addressing AMR, such as diagnostics and vaccines) and ensuring equitable access. The G7 can build on past and ongoing achievements to collaborate and unify in action against the devastating impacts of AMR and ensure a robust and sustainable supply of antibacterials and other health technologies addressing AMR.

**Let’s think ahead and act together.**

**Table 1: Country-by-Country actions**

COUNTRY	Examples of G7 actions to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market.
CANADA	<p><b>October 2022:</b> The <a href="#">Government of Canada pledged support of CAD 300,000</a> (EUR 222,000) for further developing <a href="#">SECURE</a>, a new antibiotic access initiative by GARDP and WHO.</p> <p><b>April 2023:</b> <a href="#">Canada’s Budget Plan 2023</a> contains a commitment to ‘secure new antimicrobials for Canadians’. Funding level not provided.</p> <p><b>Next Steps:</b></p> <ul style="list-style-type: none"> <li>• <b>2023:</b> Federal, provincial and territorial governments endorsed a Pan-Canadian Framework for Action on AMR in 2017 and will build on this through the publication of a Pan-Canadian Action Plan (PCAP) on AMR in 2023. The Action Plan outlines 10 priority actions to mitigate the socio-economic impacts posed by AMR. Economic and regulatory incentives are one of 10 priority action areas for the PCAP.</li> <li>• <b>June 2023:</b> Public Health Agency Canada commissioned the <a href="#">Council of Canadian Academies (CCA)</a> to conduct an examination of economic pull incentives for encouraging market entry and sustained market availability of high-value antimicrobials in Canada. An expert external advisory group was created to help answer critical questions on AMR, including developing a priority setting framework for pull incentives. The report is due for publication in June 2023.</li> </ul>
FRANCE	<p><b>Since 2015:</b> Exceptions to the Health Technology Assessment (HTA) criteria for new antibiotics in combination with exclusions from clawback mechanisms for pre-existing antibiotics. These exemptions enable price renegotiation for medicines at risk of shortages, and higher unit prices. See also <a href="#">Gotham et al. 2021</a>.</p> <p><b>Since 2017:</b> The Ministry of Health takes part in discussions with the private sector and academia within the framework of the Strategic Committee of the Health Industries and Technologies sector (CSF-ITS). Antibiotic resistance forms part of the four priorities the CSF works on. They have formed a work group, among others, that focuses on the creation of economic conditions conducive to the development and marketing of solutions to combat antibiotic resistance.</p> <p><b>January 2022:</b> France published its <a href="#">‘2022-2025 National Strategy for Preventing Infections and Antibiotic Resistance’</a>. Promotes infection prevention and control measures and antibiotic stewardship. Priorities focused on promoting innovative research, developing and maintaining products that contribute to preventing infections and controlling antibiotic resistance. This includes protecting the existing therapeutic arsenal by adopting incentives to ensure the availability of off-patent antibiotics and exploring incentive schemes that facilitate innovative products and technologies being brought to penetrate and remain on the market.</p> <p><b>2023:</b> To address the challenge of increasing shortages and lack of availability of essential off-patent antibiotics, the French Government (including five ministries and the two national medicines agencies) has requested support from the DG REFORM of the European Commission in 2020 to identify appropriate countermeasures. The project targets the root causes of the recurrent shortages and lack of availability in the human and animal sectors, while taking into account the environmental impact, in a One Health approach.</p> <p>WHO published its analysis <a href="#">report</a> in both sectors in January 2023. Further steps include the implementation and follow-up of some proposed measures (especially</p>

COUNTRY	Examples of G7 actions to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market.
	<p>in the animal sector) as well as workshops to build knowledge and capacity of the French authorities on the transfer of marketing authorization in a situation of shortages and the potential similarities and differences in the manufacturing and regulatory requirements of human and veterinary antibiotics.</p> <p><b>February 2023:</b> The French HTA authority (HAS) issued its new <a href="#">principles of evaluation of the Transparency Commission relating to drugs with respect to their access to reimbursement</a>. This document includes a focus on the evaluation of antibiotics targeting multi-resistant bacteria, with an adapted evaluation framework (p. 32). The HAS also published a <a href="#">working document</a> detailing the Commission's reflections on the evaluation of antibiotics active on highly resistant bacteria, which led to the integration of this field into the general document.</p> <p><b>Next steps:</b></p> <ul style="list-style-type: none"> <li>• <b>2023:</b> The 2016 inter-ministerial <a href="#">roadmap</a> "Controlling Bacterial Resistance To Antibiotics" is currently being updated in order to formulate strategic and ambitious proposals in a new roadmap, with a stronger "One Health" approach for the next 10 years. This update mobilizes all the inter-ministerial actors (7 ministries and 6 agencies). The updated roadmap will include a section dedicated to protecting the existing arsenal (therapeutic as well as diagnostic and preventive) by adopting incentives to ensure the availability of off-patent antibiotics and exploring incentive schemes that facilitate and accelerate innovative products and technologies being brought to penetrate and remain on the market (all of which with a One Health approach).</li> <li>• <b>2024:</b> Launching of the second EU-JAMRAI, coordinated by France.</li> </ul>
GERMANY	<p><b>Since 2017:</b> Changes in §35 SGB V &amp; Act for Fair Competition Among Health Insurance Funds in the Statutory Health Insurance Sector - GKV-FKG. Reimbursement exemption from internal price reference groups for antimicrobials addressing certain resistance patterns (as added therapeutic value). Allows higher unit prices for selected antibiotics and backs development and production of generic antibiotics.</p> <p><b>April 2020:</b> Germany grants reserve antibiotics special status in national HTA process. The pharmaceutical company does not need to prove an additional benefit of the reserve antibiotic to a comparator. This leads to an advantage in German pricing processes and eventually to an appropriate value-based pricing for new innovative antibiotics. Antibiotics qualifying as reserve and undergoing this procedure are: Cefiderocol from Shionogi, Ceftazidim/Avibactam from Pfizer, Ceftolozan/Tazobactam from MSD, Imipenem/ Cilastatin/ Relebactam from MSD and Eravacyclin from PAION Deutschland GmbH.</p> <p><b>Since 2021:</b> Germany supports the participation of two German institutions as associated partners in <a href="#">UNITE4TB</a> with EUR 25 million over seven years, aiming to accelerate and improve new and effective treatments for drug-resistant and drug-sensitive tuberculosis.</p> <p><b>April 2022:</b> The <a href="#">final report</a> of the German AMR strategy (DART2020) was published.</p> <p><b>October 2022:</b> The German Federal Ministry for Education and Research (BMBF) announced additional funding of <a href="#">EUR 50 million to support GARDP</a> over the next five years (2023-2027).</p>



COUNTRY	Examples of G7 actions to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market.
	<p><b>February 2023:</b> The German Federal Ministry of Health (BMG) presented the new draft "<a href="#">Act to Combat Supply Shortages of Off-Patent Medicines and to Improve the Supply of Pediatric Medicines</a>" (<i>Arzneimittel-Lieferengpassbekämpfungsgesetz</i> or "ALBVVG"). Reserve antibiotics with new active pharmaceutical ingredients against multi-resistant bacterial pathogens are foreseen to be significantly privileged under the revised pricing and reimbursement laws. The plans include that pharmaceutical company's freely set sales price at market launch shall continue to be reimbursed, and companies will no longer have to conduct the usual rebate negotiations with the GKV-Spitzenverband. In case of quantity expansions, such as indication extensions, price-volume agreements are envisaged.</p> <p><b>April 2023:</b> The follow up German AMR strategy (<a href="#">DART2030</a>) strategy was published, featuring a One Health focus and stronger involvement of the environment sector.</p> <p><b>Next steps:</b></p> <ul style="list-style-type: none"> <li>Germany will participate in <a href="#">The Horizon Europe Candidate Partnership: One Health AMR</a>.</li> </ul>
ITALY	<p><b>March 2022:</b> Publication of the report "Antibiotic use in Italy - 2020" provides data and analysis on the trend in consumption and expenditure of antibiotics for human use in Italy. <a href="#">AIFA publishes the Antibiotics Report 2020</a></p> <p><b>August 2022:</b> Published the <a href="#">Italian guidelines on diagnosis and management of infections caused by MDRO</a> by scientific societies, commissioned by the Ministry of Health.</p> <p><b>October 2022:</b> Italy contributed to the country profile published in "<a href="#">Addressing the burden of infections and antimicrobial resistance associated with health care</a>" by OECD.</p> <p><b>November 2022:</b> the Italian Medicines Agency (AIFA) published <a href="#">Recommendations on targeted therapy of resistant Infections</a>.</p> <p><b>February 2023:</b> Publication of the second <a href="#">National Action Plan on AMR 2022-2025</a>.</p> <p><b>April 2023:</b> Publication of the report "<a href="#">Antibiotic use in Italy - 2021</a>" provides data and analysis on the trend in consumption and expenditure of antibiotics for human use in Italy.</p> <p><b>Next Steps:</b></p> <ul style="list-style-type: none"> <li>Article 1, paragraph 529, of Law no. 197, authorized the expenditure of EUR 40 million for each of the years 2023, 2024 and 2025 to implement the measures and interventions envisaged in the NAP on AMR 2022-2025.</li> </ul>
JAPAN	<p><b>December 2022:</b> Commitment of YEN 1.1 billion (USD ~8 million) announced in Japan's 2023 fiscal year budget for a 'support program to secure antibiotics' targeting antimicrobial agents for drug resistant bacteria that pose a public health threat. The program is limited to highly effective products that have been approved and launched domestically.</p> <p><b>January 2023:</b> Japan announced a plan to ensure stable domestic supplies of priority antibiotics. Support will be provided to companies for establishing national Active Pharmaceutical Ingredient (API) manufacturing and storage facilities for</p>

COUNTRY	Examples of G7 actions to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market.
	<p>four <math>\beta</math>-lactam antibiotics (cefazolin, cefmetazole, ampicillin/sulbactam, tazobactam/piperacillin).</p> <p><b>Next Steps:</b></p> <ul style="list-style-type: none"> <li>• The three-year ‘<i>support program to secure antibiotics</i>’ is due to begin in 2023 and will provide a revenue guarantee, a compensation payment for lost profits due to antimicrobial stewardship regulation - subsidizing the difference between actual sales and forecasted size of target antimicrobials (based on expert evaluation). This is a revenue guarantee model that will ensure access to priority antimicrobials and aims to stimulate R&amp;D, and will use a Quality-of-Life Years (QALY) - based assessment for evaluating each product. Further information in Japanese available <a href="#">here</a>.</li> </ul>
UNITED KINGDOM	<p><b>May 2022:</b> UK in process of updating its 5-year national action plan ‘<a href="#">Tackling antimicrobial resistance 2019 to 2024: addendum to the UK's 5-year national action plan</a>’. The proposed changes, among other objectives aim to:</p> <ul style="list-style-type: none"> <li>- Improve the availability of data to better understand the prevalence of antimicrobial resistance across human-health and animals, and linking of this data to enable analysis of AMR and our approach to managing infection through dashboards and research</li> <li>- Reflect priorities identified by the UK AMR Research Program to explore and evaluate antimicrobial use, prescribing, new therapeutics, diagnostics, stewardship and resistance across both human health and animal, and lessons learned from COVID-19.</li> </ul> <p><b>July 2022:</b> Following implementation of a <a href="#">pilot subscription model</a>, the UK became the first country in the world to pay drug companies (Pfizer, US; Shionogi, Japan) a fixed fee per year (GBP 10 million per year for 3-10 years) for supplying antibiotics (ceftazidime with avibactam and cefiderocol). This is the first implementation of a fully delinked pull incentive globally. Payments for the new antibiotics are not linked to the volume of sales but are based on the added value to the health and social care system. The subscription model provides a known yearly revenue for the developer of the drug to ensure access, regardless of amounts used. The National Institute for Health and Care (NICE) used a Quality-of-Life Years (QALY) - based assessment valuing each drug at GBP 11-19 million per year. The level of revenue provided not only guarantees access but is aimed to render the R&amp;D of new antibacterials a more attractive proposition, encouraging innovation in the sector. It is currently too soon to evaluate whether this model has stimulated R&amp;D and innovation in the sector.</p> <p><b>November 2022:</b> <a href="#">Call for evidence</a> on the UK’s ‘Antimicrobial resistance national action plan’ published to inform the development of the next 5-year national action plan, which will run from 2024 until 2029.</p> <p><b>November 2022:</b> Publication of ‘<a href="#">Lessons learnt from the UK project to test new models for evaluating and purchasing antimicrobials</a>’ following consultation with key stakeholders.</p> <p><b>Next steps:</b></p> <ul style="list-style-type: none"> <li>• Ongoing engagement exercise with key stakeholders planned for development of a routine framework for evaluating other new antimicrobials and paying for them using the subscription contract approach. <a href="#">Plans</a> to adopt a more pragmatic approach to determine the value of the contract payments</li> </ul>

COUNTRY	Examples of G7 actions to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market.
	<p>for qualifying products. Potentially a clinical points-based scoring system that will allow aspects of value that are unique to antimicrobials to be captured.</p> <ul style="list-style-type: none"> <li>• Publication of the next 5-year AMR National Action Plan in 2024</li> </ul>
UNITED STATES OF AMERICA	<p><b>2020 - to present:</b> The Pioneering Antimicrobial Subscriptions To End Up surging Resistance Act of 2021 (<a href="#">PASTEUR Act</a>) (originally submitted in 2020) is a bill authorizing the Department of Health and Human Services (HHS) to enter into subscription contracts for critical-need antimicrobial drugs. The PASTEUR ACT would establish a Committee on Critical Need Antimicrobials which would grant upfront payments to antibiotic developers with new antibiotics that address unmet need and add significant clinical value. The current proposed value of these contracts ranges from USD 750 million to USD 3 billion over 5 to 10 years, with total funding of USD 11 billion over 10 years. The exact amounts awarded will depend on the new antibiotic and whether it has a novel mechanism of action and/or target and whether it targets a WHO priority pathogen. <b>The Act has been reintroduced to Congress in April 2023 after failing to pass last year.</b></p> <p><b>May 2022:</b> The US committed up to <a href="#">USD 300 million to CARB-X</a> over the next ten years, supporting early stage R&amp;D for new antimicrobials.</p> <p><b>March 2023:</b> <a href="#">President’s Budget Request (PBR) for fiscal year 2024</a> included USD 9 billion in mandatory funding to encourage the development of innovative antimicrobial drugs, by establishing a novel payment mechanism to delink volume of sales from revenue for newly approved antimicrobial drugs and biological products that address a critical unmet need.</p> <p><b>March 2023:</b> Publication of <a href="#">Preparing for the Next Pandemic in the Era of Antimicrobial Resistance</a> by the <a href="#">Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB)</a>, with recommendations to develop novel antimicrobials, vaccines, diagnostics, and threat agnostic platform technologies focused on resistant bacterial and fungal pathogens, which are material threats likely to arise during a public health emergency.</p> <p><b>Next Steps:</b></p> <ul style="list-style-type: none"> <li>• In the event that the PASTEUR Act is not enacted into law, HHS has begun the process required to establish a novel payment mechanism with the HHS proposed legislative program.</li> </ul>
EUROPEAN UNION	<p><b>May 2022-2025:</b> The European Commission (EC) is supporting the EU Member States to set up a new <a href="#">One Health AMR Candidate Partnership</a><sup>24</sup>, expected for launch in 2025, which will be a cornerstone of the EC’s activities in research and innovation. The aims of that partnership will be to coordinate and align national AMR research activities and investments in Europe and beyond; to boost research and innovation and promote cross sectoral cooperation on AMR with a One Health approach. The Global Health EDCTP3 Joint Undertaking (<a href="#">GH EDCTP3 JU</a>) has AMR as one of its foci (see e.g. WP 2023<sup>25</sup>).</p> <p><b>December 2022:</b> <a href="#">European Health Emergency Preparedness and Response Authority (HERA) AMR feasibility study on stockpiling</a> published. Study commissioned by European Commission DG HERA.</p>

<sup>24</sup> [https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/european-partnerships-horizon-europe/health\\_en](https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/european-partnerships-horizon-europe/health_en)

<sup>25</sup> [https://research-and-innovation.ec.europa.eu/system/files/2023-04/edctp\\_wp2023-annex1\\_calls\\_for\\_proposals.pdf](https://research-and-innovation.ec.europa.eu/system/files/2023-04/edctp_wp2023-annex1_calls_for_proposals.pdf)

COUNTRY	Examples of G7 actions to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market.
	<p><b>March 2023:</b> Final results from the HERA study on <a href="#">Bringing AMR medical countermeasures to the market</a> published. Includes a simulation of four pull incentives mechanisms (revenue guarantee, market entry reward, milestone-base reward and combination of market entry reward with revenue guarantee) and some considerations on the legal and practical implementation at the EU level. Follow-up and implementation of chosen option(s) supported by <a href="#">EU4Health Action 2023 “CP-p-23-16”</a> with a budget of EUR 22 million. Interim report published <a href="#">here</a>.</p> <p><b>April 2023:</b> The revision of the <a href="#">EU Pharmaceutical Legislation</a> has been adopted, which includes addressing AMR, as well as preventing excessive and inappropriate use of antimicrobials related provisions, in particular to encourage the development and the placing on the market of new antimicrobials and their prudent use. Two pull incentives have been proposed: a temporary mechanism consisting of transferable exclusivity vouchers for the development of novel antimicrobials to be granted and used under strict conditions, and procurement mechanisms that would guarantee revenue regardless of sales volumes to ensure access to new and existing antimicrobials.</p> <p>The Commission also adopted a proposal for a <a href="#">Council Recommendation on stepping up EU actions to combat antimicrobial resistance in a One Health approach</a>, with objectives to strengthen One Health national action plans on AMR and AMR research and innovation to foster R&amp;D, and incentives for innovation and access to antimicrobials and other AMR medical countermeasures.</p>
Other relevant initiatives of interest	
SWEDEN	<p><b>December 2022:</b> Sweden’s revenue guarantee model pilot phase finishes. The model’s main aim was to ensure national access to pre-existing and new antibiotics not being launched in Sweden due to the small market size. Compensation of at least SEK 4 million (Euros 400,000) per product per year was guaranteed to four pharmaceutical companies in return keeping a defined security stock of five antibiotics in Sweden and guaranteeing delivery to hospitals within 24 hours of ordering. The five different antibiotics are (both newly approved and pre-existing): ceftolozane/ tazobactam, imipenem/cilastatin/relebactam, cefiderocol and meropenem/ vaborbactam – newly approved antibiotics – and fosfomycin (a pre-existing antibiotic not available in Sweden). The compensation is partially delinked from sales revenue and the agreement was valid for 2 years with the possibility of extension.</p> <p><b>January 2023:</b> 1st report on the Swedish reimbursement model <a href="#">published</a>. The evaluation concluded that the model was effective in ensuring access to the selected antibiotics. The companies involved in the pilot were mostly positive, appreciating the transparency, flexibility and simplicity of the agreements, but highlighted that it was difficult to estimate suitable stock levels and that the amount of compensation was not based on the drug's societal value in terms of life years saved.</p> <p><b>Next Steps:</b></p> <ul style="list-style-type: none"> <li>The compensation level for the pilot scheme is being further investigated based on patient and sales data in Sweden and Europe. A final supplementary report is due in Spring 2023, with a recommendation to the government regarding the continuation of the model.</li> </ul>

COUNTRY	Examples of G7 actions to create economic conditions to preserve existing antibiotics and their access, strengthen antibacterial R&D, and bring new drugs to market.
	<ul style="list-style-type: none"> <li>As part of Sweden’s Presidency of the Council of the European Union, a report on <i>sustainable innovation and access to effective antibiotics</i> was commissioned and is due for publication in 2023. This is a collaboration between the European Observatory on Health Systems and Policies, the London School of Economics and Political Science (LSE), and the Ministry of Health and Social Affairs of Sweden.</li> </ul>
NETHERLANDS	<p><b>December 2022:</b> <a href="#">Non-paper concerning novel stimuli for the development and keeping on the market of antimicrobials</a>. This non-paper is based on an initiative from the Netherlands and is supported by Austria, Belgium, Finland, France, Hungary, Ireland, Latvia, Lithuania, Luxembourg, Poland, Portugal, Slovakia, and Slovenia.</p>

**Table 2: Summary of selected market incentive models/reimbursement mechanisms.** \*A non-exhaustive outline of models and reimbursement mechanisms and legislation provided. Updated from [May 2022](#)

Country/ Sponsor	Model type/ Mechanism	Status	Key Goals		Provisions		Volume (per drug)	Level of Delinkage	Time Point (dev. pipeline)	Complexity of implementation
			STIMULATE R&D & INNOVATION	ACCESS - EXISTING Abs	ACCESS - LMICS	STEWARDSHIP				
UNITED KINGDOM (UK -England)	Subscription model	ACTIVE QALY-based values for each antibiotic released 11.04.2022	✓	✓	✗	✓	Max. GBP 10 mn/yr for 3-10 yrs. (total max. GBP 100 mn) - QALY - based values indicate ~GBP 11-19 mn per year per drug	Full (fixed revenue)	Late (post approval)	Very high - new Health Technology Assessment (HTA), reimbursement & procurement processes
SWEDEN (SE)	Subscription model	PILOT ENDED (1 <sup>st</sup> review of results published)	✗	✓	✗	Partial (covered by existing provisions)	SEK 4 mn per yr (EUR ~0.4 mn)	Partial (min. guaranteed revenue)	Late (post approval)	Low
GERMANY (DE)	Changes in §35 SGB V & Act for Fair Competition Among Health Insurance Funds in the Statutory Health Insurance Sector - GKV-FKG	Since 2020  Active 1x Ab assessed - Cefiderocol	✓	✓	✗	✓	Enables higher unit prices	NA	Late (post approval)	Low based on existing regulation of innovative medicines – Pharmaceuticals Market Reorganization Act (AMNOG)
FRANCE (FR)	Price renegotiation for medicines at risk of shortages	Since 2015	✗	✓	✗	✗	Enables higher unit prices	NA	Late (post approval)	Low
UNITED STATES OF AMERICA (US)	PASTEUR ACT (Subscription model)	Not active (Resubmitted to US Congress in April 2023)	✓	✗	Partial	✓	USD 0.4-3 bn (3-5 awards – total max. USD 11 bn / 10 yrs.)	Partial (min. guaranteed revenue)	Early	High
JAPAN	Revenue Guarantee	Not Active (planned start date in 2023)	✓	✓	✗	✓	YEN 1.1 bn announced in budget for 2023	Partial (guaranteed revenue)	Late (post approval)	Low
WHO/ GARDP	SECURE	Under development	✗	✓	✓	✓	Under development			TBD

TBD: to be determined

## **Annex 1: Market incentives – overview of mechanisms<sup>26</sup>**

Pull incentives encompass a variety of mechanisms proposed including these examples:

- **Subscription Model.** Fixed annual payments or minimum revenues for a set period in return for sufficient antimicrobial product supply guarantee, delinked from the volumes sold
- **Market-Entry Reward and Monetary Prizes.** One-off or milestone-based payments to reward completed development stages (typically late-stage R&D) or market launch of new antimicrobials
- **Ongoing Revenue Incentives.** Minimum price guarantees or reimbursement system carve-outs to reflect public health effects and societal value of new antimicrobials
- **Exclusivity Extension.** Patent extensions granted to the successful antimicrobial innovator with applicability to already approved drugs (potentially tradable between firms)
- **Accelerated Approval and Priority Review Vouchers.** Vouchers for accelerated assessment and approval of antibiotics or other products under development by the same company (typically tradable between firms)
- **Tax credits.** This incentive provides tax credits to companies that invest in antibiotic research and development. This reduces the cost of development and provides a financial incentive for companies to invest in antibiotic research
- **High unit price model.** This incentive aims to ensure high revenues despite low volumes analogous to orphan drugs

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<sup>26</sup> The Case for a Subscription Model to Tackle Antimicrobial Resistance, BCG February 2022 [accessed 1<sup>st</sup> April 2023]

## Contacts:

[www.globalamrhub.org](http://www.globalamrhub.org)

Dr. Lesley Ogilvie  
Interim Secretariat Lead  
Global AMR R&D Hub

[lesley.ogilvie@dzif.de](mailto:lesley.ogilvie@dzif.de)

[www.who.int](http://www.who.int)

Dr. Alexandra Cameron  
Senior Expert, Unit Head A.I.  
Impact Initiatives and Research  
Coordination (IRC)  
World Health Organization

[camerona@who.int](mailto:camerona@who.int)

### Global AMR R&D Hub

The Global AMR R&D Hub is a partnership of countries, non-governmental donor organisations and intergovernmental organisations to address challenges and improve coordination and collaboration in global AMR R&D using a One Health approach. The Hub was launched in May 2018 and is steered by a Board of Members.

GLOBAL  
AMR R&D  
HUB



### World Health Organization

The WHO is committed to shaping the public health R&D priority setting agenda to combat antimicrobial resistance and will continue to review the preclinical and clinical antibacterial pipeline annually. In addition, WHO is expanding its pipeline analyses to include the antifungal pipeline and has conducted a bacterial vaccine pipeline review.



World Health  
Organization