



MTPConnect

MedTech and Pharma Growth Centre

Australian Antimicrobial Resistance Network

AAMRNet

Powered by **MTPConnect**

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Australian Government
Department of Industry,
Science and Resources

Industry
Growth
Centres

SUMMARY OF RECOMMENDATIONS

Antimicrobial resistance (AMR) is where infections become resistant to the drugs developed to treat them. It is one of the most critical threats to global public health we face and could take 10,000 Australian lives per year within a generation.

Urgent action and investment is needed to protect our health security from this escalating, silent pandemic.

AAMRNet is Australia's leading multi-stakeholder expert group committed to combating the global AMR threat. The network was established and is operated by MTPConnect.

AAMRNet is advocating for urgent and significant investment from the Australian Government in two specific areas to help combat the critical and urgent global threat of AMR.

1. Establish an AMR focused accelerator in Australia

- The innovation pipeline for antimicrobial medicines and technologies is not keeping pace with public health needs. **An investment of \$11 million over five years** would enable AAMRNet to establish and operate an AMR focused accelerator in Australia that would help strengthen and sustain the pipeline of new antimicrobial technologies.
- A globally connected accelerator would support Australian innovation in the AMR sector and generate a significant return to the Australian economy through the attraction of overseas funding and the facilitation of Foreign Direct Investment (FDI).

2. Invest in a Pilot Fund for Novel Antimicrobials

- Antibiotics generate low commercial returns for pharmaceutical companies, which disincentivises them to develop and supply novel antimicrobial medicines and technologies.
- Innovative funding models that pay for a continuous supply of novel antibiotics, rather than sales-based revenue, are showing promise internationally.
- An investment of sufficient funding to establish and implement an innovative reimbursement pilot program for novel antimicrobials that is fit-for-purpose for the Australian market would ensure Australians have access to life-saving antibiotics for infections that could not otherwise be treated with existing medicines.
- Current best estimates are that a subscription model in Australia would be valued at around \$7-9 million per drug per year, subject to commercial negotiations.

By taking these actions, the Australian Government would leverage the existing work and funding from the private sector through AAMRNet and take positive steps to deliver on Australia's National AMR Strategy, recommendations from the Parliamentary report, *The New Frontier – Delivering better health for all Australians*, and global calls to action from the G7. And importantly, it would help ensure Australians have fast access to the best medicines they deserve and send a strong message to the global community that it is committed to addressing this urgent public health issue.

EXECUTIVE SUMMARY

The Australian Antimicrobial Resistance Network - AAMRNet – is Australia’s leading multistakeholder expert group committed to combating the global threat of AMR. AAMRNet was established and is operated by MTPConnect, the Industry Growth Centre for Australia’s medical technology, biotechnology and pharmaceutical sector, delivering on a key recommendation of the report, [Fighting Superbugs: A Report on the Inaugural Meeting of Australia’s Antimicrobial Resistance Stakeholders](#). AAMRNet leverages MTPConnect’s networks and resources and its reputation as an independent and trusted voice for the sector, and brings together experts from industry, clinicians, and research.

AAMRNet is operated by MTPConnect with cross-sector stakeholder investment and support.

Industry contributions provided by:

- Pfizer ANZ
- CSIRO
- MSD Australia
- Botanix Pharmaceuticals
- Recce Pharmaceuticals
- GSK Australia
- SpeedX
- Medicines Australia
- Tenmile
- Biointelect
- Monash Centre to Impact AMR
- Bugworks Australia

Partner organisations:

- AusBiotech Ltd
- BiomeBank
- Community for Open Antimicrobial Drug Discovery (CO-ADD)
- DMTC Limited
- Epichem Pty Ltd
- Formulytica Pty Ltd
- GARDP – Switzerland
- Incubator for Antibacterial Therapies in Europe (INCATE)
- LBT Innovations
- Menzies School of Health Research
- Microbio
- Monash Biomedicine Discovery Institute
- Neolixir
- RESULTS International Australia
- Roche Diagnostics Australia

AMR occurs when microbes, including bacteria, parasites, viruses, or fungi change to protect themselves from the effects of the antimicrobial drugs that are designed to destroy them. The World Health Organization (WHO) has declared it one of the top ten global public health threats facing humanity and has cautioned that it is possible that a “post-antibiotic era” may be coming, where minor infections – currently easily treated with common antibiotics – may become deadly¹. It is a silent pandemic, it’s happening now, it’s getting worse, and we are ill-prepared.

AMR is also a critical threat to Australia’s health security. The Australian Group on Antimicrobial Resistance (AGAR) described AMR as “...a risk to patient safety...” and warned it may “...limit future capacity to perform medical procedures such as organ transplantation, cancer chemotherapy, diabetes management and major surgery because of a lack of effective antimicrobials”².

¹ World Health Organization. 2014. Antimicrobial Resistance Global Report on Surveillance. https://apps.who.int/iris/bitstream/handle/10665/112642/9789241564748_eng.pdf;jsessionid=FAA9126AD29D83C9BD29A1B8EA167FD8?sequence=1

² Australian Group on Antimicrobial Resistance; Sepsis Outcome Programs, 2018 Report

The COVID-19 pandemic and its health and economic impacts provide a stark reminder of the need to focus on Australia's health security and has demonstrated the importance of strengthening preparedness for global health threats such as the one posed by AMR. The threat of AMR to the health and welfare of Australians and the sustainability of our healthcare system cannot be underestimated. CSIRO Biosecurity Research Director, Dr Paul de Barro, described it as "the biggest human health threat, bar none. COVID is not anywhere near the potential impact of AMR"³.

AMR was estimated to have caused at least 1.27 million deaths in 2019, more than both malaria and HIV⁴. Globally, AMR is on track to claim 10 million lives per year and put at risk a cumulative US\$100 trillion of economic output if no action is taken by 2050⁵. The estimated annual impact of AMR on the Australian economy by 2050 will be between \$142 - \$283 billion⁶.

Australia's *National Antimicrobial Resistance Strategy – 2020 & Beyond*⁷ has identified a range of priorities to help slow the development of AMR.

The key elements included in the National Strategy are all critical to address the impact of AMR and no one element on its own will solve this global crisis. However, despite best efforts around prevention, education, surveillance, and antimicrobial stewardship (AMS), AMR will continue to occur. As a result, novel antimicrobials, vaccines, and companion diagnostics remain crucial tools for protecting the health of Australians. For example, companion diagnostics improve not only surveillance but stewardship, vaccines help reduce the burden of infectious disease and related use of antibiotics. And without effective antibiotics, it would be too dangerous to perform a range of other medical procedures such as some surgeries and cancer treatments.

Antimicrobials save lives and limbs, keep people out of hospital and shorten the length of stay for hospital inpatients.

A robust pipeline of new antimicrobials is central to combatting AMR, however the WHO has warned that the pipeline of antimicrobials is "insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance"⁸.

There is a clear, critical, and established unmet need when it comes to lack of access to, and the development and commercialisation of new antimicrobials.

There is widespread consensus that a combination of 'push' and 'pull' incentives are required to support new discovery, early clinical trials and, for medicines that show promise, suitable reimbursement assessment. Push incentives are critical to help early-stage R&D, but are on their own not enough. A stark reminder of this is Achaogen, a small company that had benefitted from push incentives to gain FDA approval for its first product to treat complicated urinary tract infections. However, less than a year after launching their product, they filed for bankruptcy after sales of less than \$1 million over that time⁹. Key to overcoming this market failure will be finding ways to fully

³ The Guardian Australia (2020): <https://www.theguardian.com/world/2020/sep/10/superbugs-a-far-greater-risk-than-covid-in-pacific-scientist-warns>

⁴ [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02724-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext)

⁵ Tackling drug-resistant infections globally. The Review on Antimicrobial Resistance Chaired by Jim O'Neill. (2016). https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf

⁶ Superbugs to trigger our next global financial crisis, OUTBREAK consortium (2020)

⁷ Australia's National Antimicrobial Resistance Strategy – 2020 and Beyond, [Australia's National Antimicrobial Resistance Strategy - 2020 and Beyond | Antimicrobial resistance \(amr.gov.au\)](https://www.amr.gov.au/australias-national-antimicrobial-resistance-strategy-2020-and-beyond)

⁸ World Health Organisation, (2019), 2019 Antibacterial Agents in Clinical Development – An analysis of the antibacterial clinical development pipeline

⁹ Medicines Australia, Department-of-Health-Australias-Antimicrobial-Resistance-Strategy-2020-and-beyond.pdf

recognise the societal value of antimicrobials through de-linking payments to companies from the volume of antibiotics sold. Market-based or ‘pull’ incentives that assist developers to bring their products to the bedside are crucial to stimulate the development of new antimicrobials and ensure patient access.

Confirming the importance of pull incentives, on 13 December 2021 the G7 Finance Ministers released a statement on Actions to Support Antibiotic Development¹⁰ aiming to strengthen G7 preparedness against the silent pandemic of AMR. The statement notes that “different factors including market failure contribute to the lack of development of new antibiotics, with no new class of antibiotic coming to market for more than three decades.” It commits all G7 members “to expedite their implementation of existing strategies... and to take additional specific and appropriate steps to address the antibiotic market failure and create the right economic conditions to preserve essential existing antibiotics and ensure their access, strengthen AMR antibiotic R&D, and bring new drugs to market where they meet identified public health needs”.

The statement outlines possible steps including “exploring a range of market incentive options, with a particular emphasis on supporting relevant pull incentives, implementing new pilot projects, contributing to new national governance structures to develop economic strategies to strengthen antibiotic development, and exploring legislative and regulatory measures”. The G7 Health Ministers¹¹ and Leaders¹² have both since echoed these calls.

The Standing Committee on Health, Aged Care and Sport has also acknowledged the seriousness of the problem. In its report; [The New Frontier – Delivering better health for all Australians](#), in which antimicrobials feature prominently, the Committee recommended the Australian Government takes strong action, including at Recommendation 27, which outlines several initiatives including:

- Develop additional reforms to data exclusivity timeframes to support research and development into new drugs and novel medical technologies in areas of unmet need.
- Consider future funding initiatives for novel drug discovery and support research and development partnerships in Australia. This would assist new drugs and novel medical technologies in early stage and pre-commercial development.
- In partnership with the states and territories, develop and implement a pilot scheme for value-based payments for new antimicrobial drugs.

The Australian Government’s expenditure on systemic anti-infectives listed on the Pharmaceutical Benefits Scheme (PBS) has reduced significantly over recent years, with annual savings of over \$2.1 billion or around 70 per cent in 2021-22 when compared with 2016-17. There is, therefore, a significant opportunity to reinvest some of those savings in initiatives to combat AMR as outlined in this Submission. In doing so, the Australian Government would leverage the existing work and funding from the private sector through AAMRNet, and take positive steps to deliver on several of the recommendations from *The New Frontier – Delivering better health for all Australians* and global calls to action from the G7. In addition, it would help ensure Australians have fast access to the best medicines they deserve and send a strong message to the global community that it is committed to addressing this urgent public health issue.

¹⁰ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1040016/AMR_-_G7_Finance_Ministers_statement_on_supporting_antibiotic_development_-_final_-_13_Dec_2021.pdf

¹¹ <https://www.g7germany.de/resource/blob/974430/2042058/5651daa321517b089cdccaffd1e37a1/2022-05-20-g7-health-ministers-communicue-data.pdf?download=1>

¹² <https://www.consilium.europa.eu/media/57555/2022-06-28-leaders-communicue-data.pdf>

AAMRNet is uniquely placed to drive action on some of these priorities and is advocating for urgent, significant investment from the Australian Government in two areas.

1. ESTABLISH AN AMR FOCUSED ACCELERATOR IN AUSTRALIA

To keep pace with rising rates of resistance, a robust pipeline of new antimicrobials is essential. Currently, and as it has been for some time, this pipeline is inadequate, with fewer than 50 antibiotics in development worldwide. This compares with more than 1,000 for cancer. To make things worse, only one in four of these potential antibiotics offer a new mechanism of action which is important to overcome resistance. This innovation deficit is not something that is quickly and easily fixed due to lengthy drug development times of between 10 – 15 years.

To support and strengthen the pipeline targeted funding is required. Priority Area 6 of the National AMR Strategy highlights the need for “...dedicated funding for the national research and development agenda, including public and private investment partnerships”, and the support of “...the translation of research findings into new approaches, applications and policies to combat antimicrobial resistance”.

The New Frontiers report calls for future funding initiatives for novel drug discovery and the support of research and development partnerships as ways to assist new drugs and novel medical technologies in early stage and pre-commercial development. The National Strategy also prioritises greater engagement, and strengthening global collaboration and partnerships. All of which could be achieved though the support of this proposal.

Early-stage R&D at research and academic institutions is supported by current government research funds, including specific funding for AMR by agencies administering the Medical Research Future Fund (MRFF) and less so by the National Health and Medical Research Council (NHMRC). However, while connections between the research sector and industry are improving, closer collaboration would facilitate product development, capture the value of the investment in the research, and position Australia as a global leader in AMR research.

AAMRNet is partnering with CSIRO to scope the establishment of an Australian AMR accelerator with the aim to be fully endorsed by CARB-X and integrated into its global network, which includes accelerators in India, Germany, the UK and the USA. CARB-X has indicated its support to integrate the proposed Australian accelerator into its network as part of its global acceleration strategy should the Australian Government support the initiative. CARB-X is a global non-profit partnership supported by several donor countries and philanthropies such as the US Government, Bill & Melinda Gates Foundation and the Wellcome Trust. It is investing US\$822 million from 2016-32 to accelerate innovation in the development of new therapeutics, vaccines, and diagnostics that address the global rise of AMR, typically up to US\$8 million for selected projects. CARB-X has demonstrated its commitment to supporting Australian projects through its funding of AMR research projects at SpeedX, and the University of Queensland (see Case Study below). CARB-X accelerators are designed to provide scientific, technical, and business support to CARB-X-applicants and funded product developers, with the accelerator network acting as a one-of-a-kind source of knowhow and expertise in antibacterial drug development, diagnostics, business strategy and other areas essential to supporting early development research projects. Importantly the Australian accelerator would be the only CARB-X endorsed accelerator in the Western Pacific Region, providing the opportunity to significantly strengthen and expand Australia’s international AMR profile and connections.

The proposed accelerator would also assist and advise Australian organisations looking to access other sources of overseas funding such as the Novo Repair Fund, INCATE, AMR Action Fund, and others.

As Australia's leading multi-stakeholder AMR expert group, AAMRNet would also provide expert advice for the Australian Government on matters of AMR policy, leveraging the leading global AMR expertise embedded in AAMRNet's team and broader membership.

Australian Government support of the proposed AMR Accelerator would further leverage not only the work AAMRNet is currently doing with CSIRO, Therapeutic Innovation Australia (TIA) and its other supporter and partner organisations, but also the additional work done in collaboration with DMTC and Biointelect to audit Australia's capabilities in AMR R&D. Australia is known for its high-quality research expertise and capabilities, but there is a lack of co-ordination of this research. The audit identified a number of Australian universities, start-ups and SMEs that are actively pursuing AMR research, and it provides an important first step to maximise the impact of these efforts and strengthen AMR R&D in Australia, by enabling the better connecting of AMR knowledge generators, investors and users through leveraging the extensive MTPConnect and AAMRNet knowledge and networks.

The impact of an Australian AMR accelerator would include:

- The creation of high-value jobs; MTPConnect would directly employ, and support three to four FTEs dedicated to the AAMRNet's activities. They would mentor and guide Australian applicants to overseas funding opportunities and promote Australian R&D capabilities to international organisations looking to access Australian expertise and infrastructure, including clinical trials capabilities. These employees would have experience in AMR policy, the development and commercialisation of AMR products, and an ability to integrate into CARB-X investment processes as required. In addition, further workforce expansion would be expected through the promotion of FDI, as well as through seeding start-up companies and providing additional support to maximise the likelihood of their commercial success.
- The provision of direct, targeted funding through a competitive process, as well as in-kind support to selected projects, making them more likely to attract further sources of funding to progress product development.
- Greatly improved likelihood of success for Australian applicants for overseas funding opportunities including CARB-X grants (up to \$15 million per project); there have been approximately 12 Australian-based applications to CARB-X but only the University of Queensland (UQ) and Speedx applications have been successful. A CARB-X endorsed Australian AMR accelerator would be well placed to increase this ratio of success. By identifying and supporting local researchers to improve the quality of their submissions, our goal would be to secure CARB-X funding for at least two Australian projects per year (approximately A\$2-3million p.a. per project).
- Facilitation of FDI; a major goal for the Accelerator would be to promote Australian fee-for-service capabilities to overseas companies seeking drug screening, pre-clinical and clinical development of novel therapeutics, diagnostic development, anti-bacterial vaccine R&D, and other support and expertise that is available in Australia. The value of these FDI projects could be in the order of \$15-25 million over five years, including overseas companies conducting Phase 1 clinical trials in Australia.
- The strengthening of global collaborations and partnerships. AAMRNet has existing partnerships with leading global organisations, and these, combined with leveraging

MTPConnect's relationships and through being part of the CARB-X global acceleration strategy would further strengthen Australia's presence in the global AMR sector.

- The building of onshore capacity by providing Australian researchers with access to, and education from leading local and global experts in the development of AMR innovations. This would include the delivery of an Australian edition of the Interdisciplinary Course on Antibiotics and Resistance (ICARe) in collaboration with the UQ Institute of Molecular Biosciences, starting in 2024. This would not only provide an opportunity to upskill local researchers in areas of AMR innovation discovery and development, but also a further opportunity for FDI by attracting students and faculty from around the globe and in particular the Western Pacific region.
- Integration of the Community for Open Antimicrobial Drug Discovery (CO-ADD) into the operations of the Accelerator, providing practical and validated antimicrobial testing support to Australian applicants for overseas funding and investment. CO-ADD is internationally recognised for helping develop new antibiotics and is included on the Global AMR R&D Hub Dashboard alongside programs such as CARB-X and IMI ENABLE. It is operated out of the same UQ group that received CARB-X funding, so would ensure that Australian applicants had the appropriate type and quality of antimicrobial data required to meet the evaluation by the CARB-X review panel. Furthermore, CO-ADD has recently taken over the Shared Platform for Antibiotic Research and Knowledge (SPARK), a global antibiotic knowledgebase established by the Pew Charitable Trusts, so could help facilitate open access sharing of Accelerator data. Another component of the CO-ADD/SPARK platform is a biobank of over 800 highly resistant bacterial clinical isolates, collected through CARB-X funding from a range of lower-middle income countries. These have undergone both whole genome sequencing and full phenotypic screening for their antimicrobial resistance profiles, with the data to be deposited within the SPARK knowledge base. The Accelerator would 1) provide access to these isolates to test the effectiveness of new therapies against challenging 'real world' strains, and 2) supplement the collection with resistant isolates sourced from Australian pathology laboratories, ensuring new therapies can treat infections caused by resistant bacteria present in Australia, and providing a genetic/phenotypic database to help track resistance in Australia.
- A key source of expert policy advice for the Australian Government.

An investment by the Australian Government of **\$11 million** over five years, would enable AAMRNet to establish a dedicated Australian AMR focused accelerator, leveraging the work that AAMRNet is already doing in its collaborations with CSIRO, TIA, DMTC and Biointelect, and could generate a significant return to the Australian economy.

CASE STUDY – Overseas sourced funding

The UQ Institute of Molecular Biosciences received two CARB-X grants totalling up to \$US13.06 million if milestones are met - the first-ever Australian project funded by CARB-X. Their research is focused on a new antibiotic - Octapeptin peptides - with one grant examining their potential as a monotherapy, and the second on their use as potentiators, where they help existing antibiotics regain their activity against drug-resistant Gram-negative bacteria by disrupting the protective cell membrane. The CARB-X funding also allowed the UQ researchers to collect and characterise over 800 highly resistant clinical isolates from low-to-middle income countries, and to provide training and equipment to enable collaborators in those regions to conduct whole genome sequencing.

CASE STUDY – Foreign direct investment

Bugworks (India), a supporter of AAMRNet, which received an initial investment from CARB-X of up to US\$2.6m with potential option payments up to US\$3.6m, recently established an Australian subsidiary to support a Phase I clinical trial program for its new antibiotic. Trials such as this can involve a direct spend of around \$3-4 million and provide employment for up to 15 highly qualified professionals.

2. INVEST IN A PILOT FUND FOR NOVEL ANTIMICROBIALS

Australians deserve access to the new and much needed antibiotics to ensure their ongoing health security. AAMRNet is proposing the Australian Government allocate sufficient funding to establish and implement an innovative reimbursement pilot program for novel antimicrobials for the Australian market. The pilot would provide the critically needed ‘pull’ incentive called for by the G7 in order to overcome the market failure that is hindering the development and commercialisation of novel antimicrobials. It would also deliver on a recommendation of the Parliamentary report *The New Frontier – Delivering better health for all Australians*, which calls for a pilot scheme for value-based payments for new antimicrobial drugs to be developed and implemented.

This is a unique opportunity for government, clinicians, researchers, and industry to work together on practical solutions for an urgent health security risk. A simple, pragmatic approach can be found which would signal Australia’s commitment to tackling the growing threat of AMR and ensure we are at the cutting edge of this effort globally.

AAMRNet would leverage the expertise and networks of its supporters and partners to bring together key relevant stakeholders to consider options for adapting international exemplars to design a model for a pilot fit for purpose for Australia.

Why a new funding model is needed

DRIVE-AB (Driving Re-Investment in R&D and responsible AntiBiotic use) was a public-private, collaborative multinational consortium funded by the European Innovative Medicines Initiative to recommend options to stimulate innovation and responsible use while ensuring global access to novel antibiotics to meet public health needs. Its final report highlighted that “new economic models that create incentives for the discovery of new antibiotics and delink the return on investment from volume of sales are long overdue”¹³.

Australia, like other countries, has multiple challenges facing companies that invest in the development of novel antimicrobials:

- Uptake of novel antimicrobials is slow as they are typically held in reserve by healthcare practitioners until resistance to older treatments has emerged, and when they are used, it is only in acute situations and for short course dosing regimens. This immediately limits the usage of a new product and the ability to recoup R&D and commercialisation costs. These barriers are not faced by therapeutics used as longer course treatment regimens for chronic conditions such as cancer or heart disease.
- There is no nationally consistent reimbursement system for antimicrobials in Australia. There are multiple payers with regard to novel antimicrobials and the payer will depend not only on

¹³ DRIVE-AB, Novel business models needed to revive reinvestment in antibiotics http://drive-ab.eu/wp-content/uploads/2015/07/Novel-business-models-needed-to-revive-reinvestment-in-antibiotics_Ursula_Biotechnology-Journal.pdf

the PBS status of the drug, but also on individual patient circumstances. For example, state governments will bear the cost of treatment for public hospital inpatients. However, in private hospitals, the payer could be the patient, insurer, hospital, or the Federal Government when the antimicrobial is listed on the PBS and prescribed in accordance with PBS restrictions.

- Constrained hospital budgets can mean that the use of novel antimicrobials may be discouraged for financial reasons, even when they may be a more clinically appropriate treatment for a patient than a generic antimicrobial¹⁴.
- There is a lack of rapid point-of-care diagnostics to identify which patients need immediate access to newer antimicrobials and which can be treated with generics.
- Novel antimicrobials are generally undervalued by reimbursement systems relative to the benefits they bring to society as indispensable, life-saving drugs. This is because of the existence of low-cost, often generic comparators which are still effective for many infections, and the inherently narrow focus of health technology assessment (HTA) on direct health costs and benefits. While it may be appropriate for most therapies to maintain that narrow focus, the societal benefits of having a supply of novel antimicrobials requires a broadening of the HTA perspective. Indirect costs, such as delays in surgical procedures for patients with AMR, need to be considered in estimating the value of new antibiotics. Additionally, longer term direct health costs associated with development of complications of AMR, such as patient readmissions to hospital and extended lengths of hospitalisation need to be considered in HTA.
- Precision medicine is more important than ever in antimicrobial therapy, but regulatory and reimbursement challenges based on clinical indications exist. Developing a precise (narrow spectrum) therapy for a specific bacterial pathogen is economically unattractive under the current Australian reimbursement model. However, development of targeted precision-focused therapy is imperative to control the collateral selection pressure that is driving AMR development.

New funding approaches in UK, Sweden and US provide exemplars for Australia to consider

In order to improve Australian's access to new antimicrobials and help stimulate the 'broken market' a new approach to funding is urgently needed. The UK National Institute for Health and Care Excellence (NICE) recently launched a pilot program using a 'de-linked' model in which companies are paid an annual subscription fee to supply as much or as little of an antimicrobial as required. This 'insurance' results in more predictable revenue for the manufacturer and predictable access to urgently needed medicines for the health system. In other words, companies are paid for antimicrobials based on their expected value to the health system and population as a whole, as opposed to the volume used.

In Sweden, a new reimbursement model is being piloted which aims to ensure the availability of new antibiotics of special medical value with market protections in force. Sweden, like Australia, is a small market and has a low, but growing level of resistant infections. Also like Australia, it struggles to attract pharmaceutical companies to make their products available in the country. Under the pilot, pharmaceutical companies will, in exchange for a guaranteed supply volume of the originator antimicrobial, receive a minimum guaranteed annual revenue from the Public Health Agency of Sweden (PHAS), based on the cost of an estimated security stock amount. Regional health departments continue to buy and pay as usual for the products, and if the actual revenue from those sales is lower than the guaranteed income for a given year, the difference will be paid from the national level. If, on the other hand, revenue from the sales exceeds the guaranteed level for a given

¹⁴ Bhatti, T et al 2018, A Perspective on Incentives for Novel Inpatient Antibiotics: No One-Size-Fits-All, Journal of Law, Medicines and Ethics, p60

year, to ensure the attractiveness of the PHAS model, a bonus equal to the price of buying 10 per cent of the security stock amount will be paid¹⁵.

In the US, the Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act also proposes a model that would provide market incentives for life-saving antimicrobial therapies. Under this Act, the US government would provide a subscription payment similar to the UK model, but larger (proportionate to the relative size of the US economy) and based on clear Target Product Profile characteristics rather than the HTA used by NICE. Developers would be paid annual, contractually agreed amounts for a duration ranging up to the antimicrobial's patent life. The government would offer developers an upfront payment for access to their eligible antimicrobial and would consider the clinical need and novelty of the therapy. Under this proposal, patients in the US insured by national payer plans (Medicare or Medicaid) would have access to PASTEUR Act antimicrobials at no additional cost to the government. The Act would also provide education on stewardship to facilitate appropriate use of new antimicrobials. A paper recently published by the Center for Global Development in 2022 estimates that globally, and over 30 years, the potential impact of the PASTEUR Act would be the saving of 9.9 million lives and showing a return on investment of 125:1¹⁶.

Other approaches that have been proposed internationally include the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) Act in the US¹⁷, and a market entry reward based on susceptibility, with a staged bonus for antimicrobial developers when resistance to their drug remains low over time¹⁸.

Some of these countries are also exploring the feasibility of using environmental criteria in decision making on antimicrobial procurement. This is designed to encourage manufacturers to ensure their products meet international standards that limit or eliminate antimicrobial pollution into the environment from the manufacture of antimicrobials themselves.

Elements of all these new approaches could be considered for possible incorporation into an Australian pilot.

A Pragmatic Valuation Approach

Countries around the world are looking at how to tackle the challenge of bringing novel anti-infectives to market. The UK has already spent several years developing a workable model to determine the expected value¹⁹ which takes into account their full value to society, including spectrum value, transmission value, enablement value, diversity value and insurance value (STEDI). This work is ongoing, as they acknowledge the need for balance between the difficulty of the task, the complexity of the modelling required and the use of expert opinion. Australia, through AAMRNet, could consider these developments and how these might be pragmatically adapted for use within Australia's HTA processes.

¹⁵ Gotham D et al. Reimbursement models to tackle market failures for antimicrobials: Approaches taken in France, Germany, Sweden, the United Kingdom and the United States <https://www.sciencedirect.com/science/article/pii/S0168851020302980#bib0140>

¹⁶ <https://www.cgdev.org/sites/default/files/ambitious-usg-advanced-commitment-subscription-based-purchasing-novel-antimicrobials.pdf>

¹⁷ <https://www.congress.gov/bill/117th-congress/house-bill/4127/text?r=10&s=1>

¹⁸ Morel, C.M., Lindahl, O., Harbarth, S. et al. Industry incentives and antibiotic resistance: an introduction to the antibiotic susceptibility bonus. *J Antibiot* 73, 421–428 (2020). <https://doi.org/10.1038/s41429-020-0300-y>

¹⁹ Rothery, C., Woods, B., Schmitt, L., Claxton, K., Palmer, S., Schulper, M., 2018, *Framework for Value Assessment of New Antimicrobials. Implications of alternative funding arrangements for NICE Appraisal*. EEPURU, Policy Research Unit in Economic Evaluation of Health & Care Interventions, viewed 17 December 2019 <<http://www.eepru.org.uk/wp-content/uploads/2017/11/eepru-report-amr-oct-2018-059.pdf>>

Current best estimates are that a subscription model in Australia would be valued at around \$7-9 million per drug per year.

Proposed principles for an Australia pilot

The following principles could be considered for inclusion in an Australian pilot.

1. The pilot could use the **de-linked model** whereby an annual subscription fee is paid regardless of the amount of antimicrobial used.
2. The pilot could incorporate regulatory and reimbursement incentives for qualified infectious disease products (QIDP), such as market entry rewards and additional market exclusivity.
3. The pilot should be **jointly supported by the Australian and State and Territory Governments**. Joint funding models already exist (such as the National Blood Authority). The framework of the National Health Reform Agreement may also provide a basis for such funding
4. The pilot could be reserved for up to five drugs which treat organisms for which the impact of resistance is high in the hospital setting. For example, carbapenem-resistant *Pseudomonas aeruginosa* is a priority 1 pathogen according to the WHO²⁰ and is a major emerging AMR threat in Australia²¹. Novel antibiotics to treat this pathogen are available but they are expensive compared to cheaper generic options so can be under-used, even when they are the most appropriate choice. In the US, the Food and Drug Administration (FDA) has granted IV cefepime-taniborbactam (under development by VenatoRx and with activity against Carbapenem-resistant *Pseudomonas aeruginosa*) QIDP.
5. The pilot should ensure **equity of access** to the chosen drugs across metropolitan, regional, rural and remote Australia, in all states and territories.
6. The pilot should support the AMS principle of using the right drug for the right patient, for the right organisms, at the right dose and formulation, at the right time, so that usage is always based on clinical need and appropriate use rather than the cost. This is consistent with infectious disease AMS which results in positive impact on patient outcomes.
7. The pilot should recognise the **broader social value** of making novel antibiotics available, including the STEDI values, while at the same time preserving their use according to AMS principles.
8. The pilot should act as a signal to industry that the government is willing to create **a stable market for novel antimicrobials**.
9. The pilot should establish **Australia as an AMR policy leader** by providing an example for other countries to follow to help address the growing, global threat of AMR.
10. Metrics should be developed and aligned on across all stakeholders to measure the outcomes of the pilot, such as hospitalization/ healthcare costs in the respective region. The outcomes will help to refine, if needed, the design of the pilot moving forward.
11. The pilot should **support international efforts** through bodies like the G7, G20 and Global Leaders Group on AMR to assist in establishing environmental standards for the manufacture of antibiotics through incentives and standards in the purchasing and reimbursement of antibiotics by the Australian and State and Territory Governments.

The short-term benefit of such a pilot is that up to five novel antibiotics could be available for clinicians to prescribe to the right patient at the right time with no budget constraints.

²⁰ <https://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/>

²¹ Williamson, Deborah. A., Howden, Benjamin P., Paterson, David L., 2019, *The risk of resistance: what are the major antimicrobial resistance threats facing Australia?* Medical Journal of Australia

The long-term benefit of such a pilot is that it would send a strong signal to the market that there is a reliable return for investing in antimicrobial R&D and would serve as an example for other countries to act.

AAMRNet is committed to working with government to help re-stimulate the market for these crucial therapies and is most appropriate due to the combined national and international expertise of its members and stakeholders.

ABOUT AAMRNET

AAMRNet, Australia's first Antimicrobial Resistance Network, was launched on 24 September 2020. It is an industry-led, inclusive collaboration of stakeholders, all committed to addressing the impact of antimicrobial resistance (AMR) on human health. In response to a key recommendation of the report, "Fighting Superbugs"²², AAMRNet was established and is operated by MTPConnect with the support of Pfizer ANZ, CSIRO, MSD Australia, GSK Australia, Botanix Pharmaceuticals, Recce Pharmaceuticals, Speedx, Medicines Australia, Tenmile, Biointelect, Monash Centre to Impact AMR and Bugworks Australia. Its members and stakeholders include universities, not-for-profits, researchers, SMEs and large multinational companies, industry peak bodies, clinicians, patients, government, and regulators. AAMRNet provides a unified voice to support and promote Australia's role in the global fight against the growing threat of drugs resistant infections. As the only body in Australia able to provide whole-of-sector representation, AAMRNet is uniquely placed to promote Australia's role in the fight against AMR and help inform government priorities and strategies.

MTPConnect established and operates AAMRNet with commitments totalling \$469,367 from its Growth Centres Project Fund Program. These, combined with matched funds from industry partners of almost \$800,000, provides significant opportunity for government to leverage any future funding of AAMRNet with existing industry funds.

Through its partnerships and engagement with key international stakeholders, AAMRNet is established as the key organisational contact point for access to Australian AMR expertise.

AAMRNet aligns its activities closely with current Australian Government priorities. Including:

- The Medical Research Future Fund (MRFF), which describes the need for collaborative, multidisciplinary research in AMR, "critical".
- The National AMR Strategy, which outlines seven objectives to address AMR, including greater engagement and collaboration.
- The National Preventive Health Strategy, which identifies AMR as an emerging threat where Australia may wish to increase its preparedness.
- The National Manufacturing Priorities, which includes medical products.
- The Department of Industry Science and Resources (DISR) Industry Growth Centre Initiative by working, as it relates to AMR, to:
 1. optimise the regulatory and clinical trials environment,
 2. boost commercialisation through increasing collaboration,
 3. improve access to global alliances, supply chains and markets,
 4. improve management and workforce skills.

AAMRNet is taking significant action on its strategic priorities to combat AMR. These include:

1. In collaboration with DMTC and Biointelect; undertaken an audit of the Australian AMR R&D landscape,
2. in collaboration with CSIRO, scoping the potential establishment AMR focused accelerator for Australia,
3. in collaboration with CSIRO, developed a report on how to better measure the real impact of AMR on mortality in Australia²³,

²² MTPConnect. 2020. 'Fighting Superbugs: A Report on the Inaugural Meeting of Australia's Antimicrobial Resistance Stakeholders'

²³ https://www.mtpconnect.org.au/images/AMR_Impact_Report_2022.pdf

4. leveraging the expertise of its membership, developed a position statement on pricing and reimbursement that considers innovative funding models and ways of better valuing antimicrobials to support patient access and incentivise R&D, and commercialisation in Australia²⁴,
5. in collaboration with TIA, delivered an AMR-focused round of its Pipeline Accelerator scheme, providing expert advice to applicants and awarding three vouchers to researchers from CSIRO, the Doherty Institute and the Murdoch Children’s Research Institute to help advance their projects,
6. in collaboration with CSIRO and CRC-SAAFE, progressing work exploring the challenges regarding the impact and removal of antimicrobial residues from water from a One Health perspective,
7. in collaboration with Evohealth, developing a report examining the critical issues raised in *The New Frontier - Delivering better health for all Australians report*, including policy options for reform of Australia’s data exclusivity framework, new funding initiatives to support novel antimicrobial technology R&D and design of a pilot scheme for value-based payments for new antimicrobials to help ensure better patient access,
8. in partnership with the UQ Institute of Molecular Biosciences, working to deliver an Australian edition of the Interdisciplinary Course on Antibiotics and Resistance (ICARe) in 2024,
9. working to develop a report on the impact of AMR on indigenous and remote populations.

To successfully combat AMR, collaboration is crucial, and the key stakeholders are many and varied. AAMRNet includes and engages with key relevant Australian and global stakeholders across the health and medical research sector, the biotechnology and pharmaceutical industry, clinicians, government, and regulators. The result is the only Australian network that links all these key stakeholders together.

AAMRNet has a robust governance framework, being guided by a steering committee co-chaired by Stuart Dignam and Andrew Bowskill from MTPConnect and comprising leading AMR experts from industry and academia including Professor David Paterson from the UQ Centre for Clinical Research, David Grolman from Pfizer ANZ, Paul Field from GARDP, Julie Phillips from Opal Biosciences, Professor Geoff Coombs from the Australian Society for Antimicrobials, Branwen Morgan from CSIRO Minimising AMR Mission, Jenny Herz from Biointelect, Merrin Tulloch from MSD Australia and Elizabeth de Somer from Medicines Australia.

Building on MTPConnect’s achievements as a trusted and independent voice to inform government on key issues, challenges and opportunities, AAMRNet has demonstrated it has the skills, knowledge and experience to provide expert advice to the Australian Government.

AAMRNet, as the only body in Australia able to provide whole-of-sector representation, is uniquely placed to promote Australia’s role in the fight against AMR, help inform government priorities and strategies, and provide the Australian Government with, within a single forum, critical access to the key opinion leaders working in the AMR sector in Australia.

AAMRNet is ideally placed to work closely with the Australian Government to deliver progress on its commitment to combat AMR.

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²⁴ https://www.mtpconnect.org.au/images/AAMRNet_PositionStatement_PricingReimbursement_2022.pdf



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