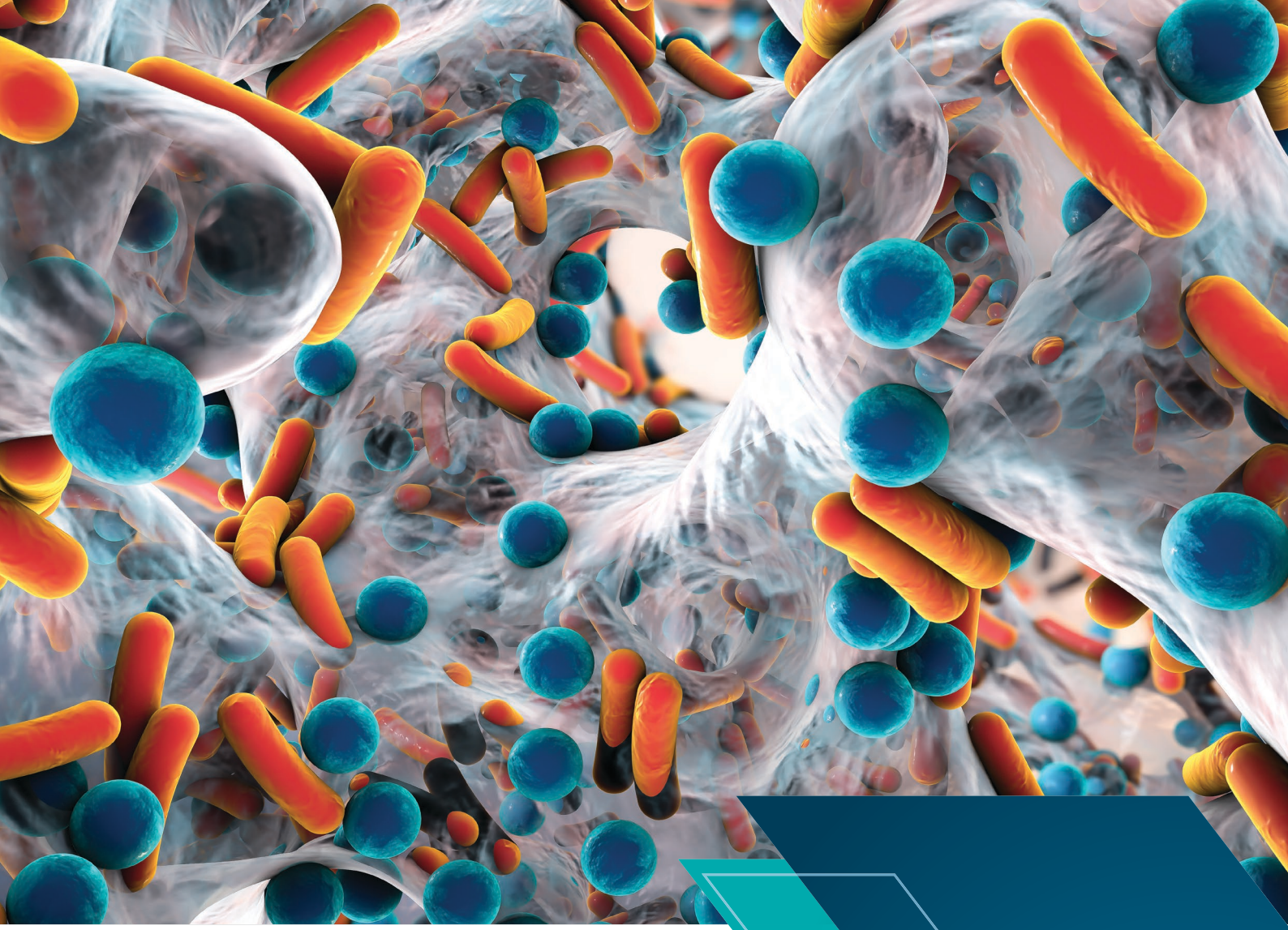

MTPConnect
MedTech and Pharma Growth Centre

FIGHTING SUPERBUGS

A Report on the Inaugural Meeting of Australia's Antimicrobial Resistance Stakeholders

September 2020

Australian Government
Department of Industry, Science, Energy and Resources

Industry Growth Centres

CONTENTS

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1 FOREWORD

MTPConnect
MedTech and Pharma Growth Centre

Simply put, antimicrobial resistance or AMR is drug resistance. It occurs when microbes such as bacteria become resistant to drugs which once killed them. They are evolving faster than researchers can invent new drugs, turning into untreatable 'superbugs'.

There are already some infections which are impossible to treat. The Organisation for Economic Co-operation and Development estimates that an average of 290 people die each year in Australia due to infections from eight resistant bacteria. This is likely an underestimation because AMR deaths can be hidden behind other conditions. Nonetheless, they also estimate that by 2050, as many as 10,000 Australians will die due to AMR. Extrapolated globally, AMR is on track to claim 10 million lives per year by 2050[1].

These are the stark statistics which prompted the United Nations Interagency Coordination Group (IACG) on Antimicrobial Resistance to declare AMR a "global crisis" and warn that "unless the world acts urgently, antimicrobial resistance will have disastrous impact within a generation[2]."

The need for new treatments is serious and urgent, a fact reinforced during the COVID-19 pandemic where many patients have died because of secondary bacterial infections[3]. Yet, as of September 2019, only 6 out of 50 antibiotics in clinical development could be classified as innovative antibiotics targeting the World Health Organization (WHO) priority pathogens[4].

In November 2019, MTPConnect convened a multi-disciplinary workshop to bring together key stakeholders from the health and medical research sector, the biotech and pharmaceutical industry, government and regulators to assess the challenges and see what could be achieved. This report details those discussions and makes a series of recommendations for new and improved approaches to addressing drug resistance. One thing is for certain: collaboration is the key.

Through Howard Florey and his Nobel prize-winning work developing penicillin into an antibiotic treatment, Australia has played a key role in the antibiotic revolution of human health, and our researchers, entrepreneurs and industry players can do it again in the fight against antimicrobial resistance.

We thank all those who attended our workshop and generously shared their expertise and insights and we look forward to many more discussions as Australia leads the way on collaboration to tackle antimicrobial resistance.

Dr Dan Grant
Managing Director & CEO

Dr Dan Grant
Managing Director & CEO

2 EXECUTIVE SUMMARY

In June 2015, the Australian Government released the First National Antimicrobial Resistance Strategy 2015-2019. Following an extensive consultation process[5] and sector input, an updated plan, for 2020 and beyond[6], was released in March 2020.

The national strategy has seven objectives, broadly covering increasing public awareness of AMR, infection prevention, responsible antibiotic distribution and international collaboration. It also deals with research and promoting investment in discovery and development of new products.

Industry is a key contributor to addressing the AMR challenge because of its expertise in product research and development, as manufacturer and supplier of products to combat AMR and through its role supporting product-related education and antimicrobial stewardship[7].

Market failure for novel antibiotics is recognised as a significant challenge. The lack of commercial return for antibiotic development has led to most pharmaceutical companies exiting infectious diseases product development and a weak pipeline of new products.

Despite this, there are green shoots of activity, such as the recent Roche Pharmaceuticals partnership with San Diego-based biotechnology company, Forge Therapeutics, to progress a novel antibiotic for the treatment of serious lung infections. There are also a small number of companies active in Australia in AMR including small medical technology and biotechnology companies as well as large multi-nationals. There is therefore an opportunity for the medical technology, biotechnology and pharmaceutical (MTP) sector to contribute to the implementation of the new national strategy and to help support development of an Australian-specific sector action plan that capitalises on both global and local industry capability and Australia's strengths in infectious diseases research.

While recognising the critical importance of infection prevention and control, promotion of prudent use of antimicrobials in humans and animals, enhanced surveillance systems and data collection and better public and professional understanding of AMR, the MTPConnect-sponsored workshop of November 2019 focused on product development gaps and strategies for incentivising investment and addressing market failure in antibiotic R&D.

The workshop, facilitated by Biointelect's Jennifer Herz and David Grainger, brought together for the first time key players from across the AMR sector – researchers, industry, clinicians and government. The interest in the issue was clear, as demonstrated by the participation of then Commonwealth Chief Medical Officer, Professor Brendan Murphy (now Secretary of the Department of Health). The workshop recommendations represent a cross-sectional roadmap for decisive action on AMR and are displayed in Table 1.

Table 1: Summary of Recommendations

Recommendations	Proposed Steps
Development of a National AMR Research Agenda	• Whole-of-government approach • Leveraged expertise from different stakeholders • National capability audit
Establishment of an Australian AMR Network	• Active participation in and collaboration with international alliances • Fit-for purpose framework to ensure better data sharing as well as resource integration and allocation • Facilitating the exchange of information and resources • Recognition of the role of human health pharmaceutical R&D industry • Review and due diligence of partnerships • Education and advocacy
AMR-Specific Streamlined Pathways	• Orphan drug category be adapted to allow for antimicrobials to be considered • Fast track process specifically for antimicrobials/priority review vouchers
Regulatory Incentives	• Additional market or data exclusivity • Waiving of registration fees • Facilitation of the repurposing of existing drugs • Facilitation and expedition of the regulation of companion diagnostics
Review of Trial Requirements	• Clinical trial design • Patient enrolment • Levels of data to support approvals • Indications
Pricing and Health Technology Assessment (HTA) Reform	• Inclusion of additional values of novel antimicrobials for wider health benefits • Price premiums over low cost generics • Setting of a minimum price level for antimicrobials to increase the pricing bar • PBS list price to be automatically readjusted when there is sole supply
New Reimbursement and Procurement Models	• Alternative payment schemes including models where payments are de-linked from sales volume • Accelerated PBAC review • Special provisions/exemptions • Listing new antimicrobials under a different formulary • Diagnostic reimbursement incentive • Reimbursement pathway to differ depending on setting • Creation of a separate insurance fund
Better Data Collection and Collaboration	• Comprehensive information on usage, epidemiology and patient outcomes to be collected • Industry to participate in initiatives related to stewardship and optimal prescribing • Ongoing collaboration among different stakeholders

3 ANTIMICROBIAL RESISTANCE: THE CLOCK IS TICKING

There is an increasing rate of resistance to many commonly used antibiotics observed through Australian surveillance programs.

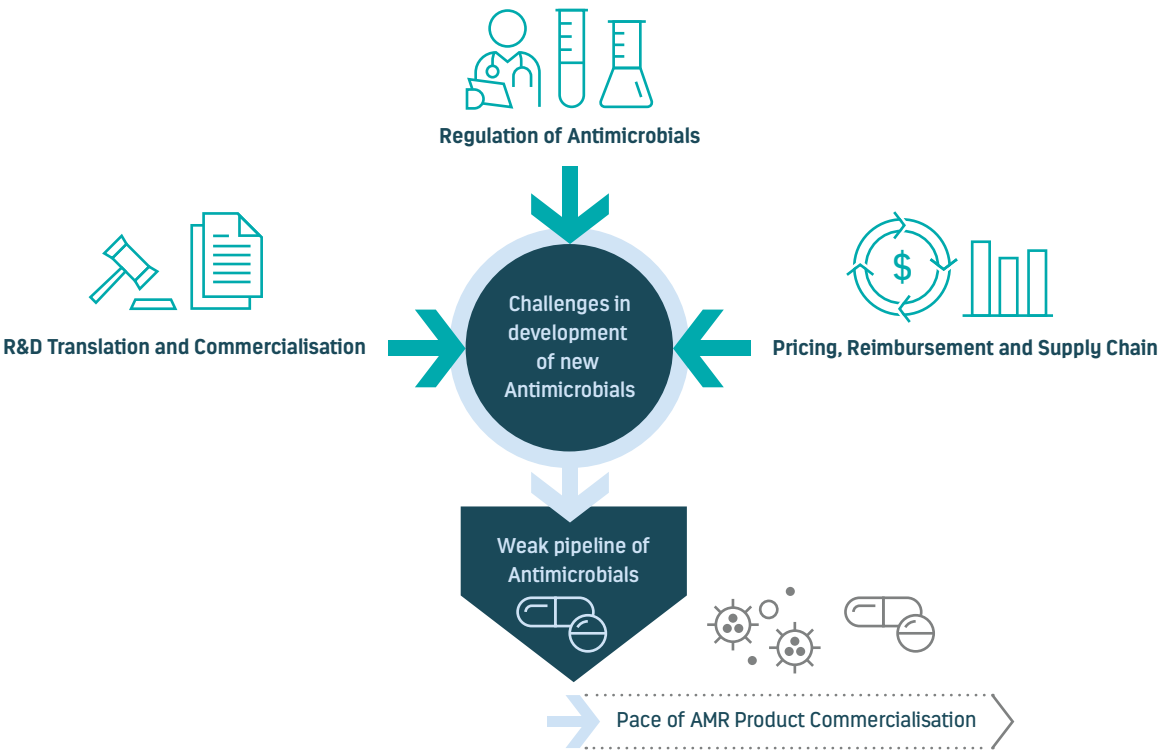
Specific pathogens that are either resistant or emerging as resistant to first and second line antibiotics are reported in Australia (Enterobacteriaceae, Enterococcus species, *Neisseria gonorrhoeae, Staphylococcus aureus, Streptococcus pneumoniae*), with the rate of *Enterococcus faecium* resistance to vancomycin, methicillin or penicillin being among the highest in the world[8]. Although resistance rates are on the rise, there has been a 'lack of urgency' to tackle AMR.

The emergence of the COVID-19 pandemic serves as a stark reminder of the need for action on AMR, with evidence that approximately 50% of patients in Wuhan, China with COVID-19 who have died had secondary bacterial infections[9]. These outcomes are consistent with previous pandemics. For example, during the 2009 H1N1 influenza (Swine flu) pandemic, secondary bacterial pneumonia resulted in an increase in hospital pneumonia cases and was identified in 29–55% of mortalities[10]. And most fatalities in the 1918 influenza outbreak were due to subsequent bacterial infection, particularly with *Streptococcus pneumoniae*[11].

As resistance to antibiotics increases, these infections will require a range of antibiotic treatment options to prevent growing rates of mortality. Recently, antibiotic use has been shown to be very high (91.3%) among patients with COVID-19 who are admitted to intensive care/high dependency units[12]. Compounding this issue, despite the urgent requirement for novel antimicrobials there has been a substantial decline in the number of companies undertaking antimicrobial development over the past two decades[13]. Three main areas have been identified as significant challenges to the development of new antimicrobials:

- R&D Translation and Commercialisation
- Regulation of Antimicrobials
- Pricing, Reimbursement and Supply Chain

These themes, and how Australia can capitalise on existing international collaborations, were explored in the workshop.



4 R&D TRANSLATION AND COMMERCIALISATION

A critical strategy to tackle AMR is to increase basic research (i.e. new preclinical models and novel mechanisms of action)[14]. However, lack of research and development translation in AMR around the world stems from the low return on investment that disincentivises commercialisation.

Funding clinical trials of prospective antimicrobials is very costly. Operational costs of Phase I to III clinical trials of an antibiotic are estimated to be upwards of $130 million, with post-approval follow-on trials costing an additional $150 million[15] where only a small portion of clinical trials will yield a marketable product. Add to this the post-marketing surveillance costs and small- and medium-sized enterprises (SMEs) seeking to enter the AMR space are often unable to attract the capital to invest in promising candidates.

For bigger companies invested in AMR research, incentives are seen as inadequate due to downward price pressure (due in part to the low prices and low perceived value of available generic antibiotics) versus the high cost of developing new technologies and the reluctance of hospitals to add the new products to their formularies.

The net present value of the average antibiotic R&D has been estimated to be negative $50 million as compared to $1.15 billion and $720 million for musculoskeletal and neurologic R&D projects respectively[16]. In other words, costs will exceed projected earnings and the investment in antibiotic R&D will be loss-making.

Return on investment is limited by relatively low sales volumes caused by the characteristics of the clinical use of antibiotics (short treatment durations inherent in antibiotic therapy) and local antimicrobial stewardship programs that limit the use of antibiotics. Truly novel compounds are held in reserve for rare infections caused by the most highly resistant strains of bacteria and see an even lower clinical application. Therefore, although new antibiotics are desperately needed, they will only maintain efficacy if they are used sparingly. Further, their use will need to be monitored closely to avoid emerging resistance, as the more they are used, the less effective they become.

This judicious use of antimicrobials, essential to the preservation of the effectiveness of existing antimicrobials for high quality patient care, along with the other reasons highlighted above, means that developing and commercialising a novel antibiotic does not currently justify the financial investment required.

Economic Challenges, Risk Return and Resourcing

- Inability to raise funds to run trials and move products along the commercialisation pathway
- Inadequate return upon commercialisation due to limited price and sales volume

It is this 'market failure' which is the major barrier in antimicrobial R&D translation and commercialisation around the globe. Although the 2017 G20 summit committed to 'further examine practical market incentive options' for R&D, there was lack of forward momentum with concrete steps[17]. International initiatives are addressing this gap and looking at pull-incentives (e.g. UK).

Case study

Economic Crisis of Antibiotic Developers Stifling New Drug Development

Founded in 2002, Achaogen was an antibiotics company, having spent more than 15 years and a billion dollars to gain FDA approval for its first product, Zemdri (plazomicin) to treat complicated urinary tract infections. The drug was approved by the FDA in June 2019, however by then, Achaogen's stock price had approached zero and funds needed for commercialisation and additional post market studies could not be met, dragging the company to bankruptcy. Another antibiotic start-up Aradigm has also teetered toward insolvency, and major players such as pharmaceutical giants Novartis and Allergan have withdrawn from antimicrobial research, showing that Achaogen has not been the only company to abandon the antibiotics sector.[18]

4.1 Further Challenges: Australian Context

Australia is known to have high quality research skills and capabilities, however there remains a significant gap between preclinical research and commercialisation. This stems from a lack of pre-clinical development capability, Good Manufacturing Practice (GMP) manufacturing and scale-up, and limited early stage collaboration between stakeholders including universities, research institutes, industry, government, health professionals and the community.

Early stage R&D at research and academic institutions is supported by current government research funds. The National Health and Medical Research Council (NHMRC) has allocated specific funding for AMR, with $201.3 million invested over the last 10 years (2009-2018) across 299 grants, more than half of which was allocated to basic science investigations, followed by $51.4 million to clinical medicine[19]. However, while connections between the research sector and industry are improving, including through projects supported by MTPConnect, further innovation is required to ensure the industry's resources, expertise and experience in bringing new products to the market are fully utilised.

On the other hand, the absence of a national AMR research agenda to guide drug development, diagnostics and surveillance results in inconsistent prioritisation and insufficient utilisation of professional skills across different sectors. Further defining how the MTP and health sectors collaborate to better meet the objectives outlined in the new National Strategy that focus on usage, prevention, surveillance and response may also be helpful in managing AMR.

The Antimicrobial Use and Resistance in Australia (AURA) Surveillance System has generated a comprehensive annual report with national surveillance data, however, challenges remain around lack of data, especially from small health services in remote areas and passive surveillance in some territories and private sectors[20]. The current surveillance system can be further improved by more routine, rapid and real-time diagnostics, the use of which can be supported by policy, practice and reimbursement.

Gap Between Research and Commercialisation

- Lack of scale-up in pre-clinical and clinical research
- Lack of collaboration between different stakeholders
- Absence of a national AMR research agenda
- Relatively low level of patient understanding and advocacy

Public awareness and education of the significant risks and the potential serious consequences of AMR are also inadequate. As a result, there are few patient groups and a relatively low level of advocacy on this topic compared to other diseases.

4.2 International Partnerships

There are several research networks that aim to collaborate and advance the development of medicines addressing infectious diseases. Australia's engagement in AMR has been variable and opportunities exist for increasing engagement with international stakeholders.

Limited International Engagement

- Variable international engagement that limits ability to tap into international funds and resources

For example, NHMRC is a member of the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R), a network which brings together 29 worldwide research funding organisations[21]. However, there are numerous other global and regional AMR-related alliances in the form of public-private partnerships involving industry, government and not-for-profit organisations, including the newly announced AMR Action Fund, a partnership of over 20 leading biopharmaceutical companies which expects to invest more than US$1 billion to bringing 2-4 new antibiotics to patients by 2030. Some others are listed in Table 2 below.

Table 2: Examples of AMR-related initiatives and alliances

Alliance	Region	Description/ Output to date
amr INDUSTRY ALLIANCE UNITED AGAINST ANTIMICROBIAL RESISTANCE	Global (over 20 countries)	A coalition of over 100 biotechnology, diagnostic, generics and research-based biopharmaceutical companies and trade associations established in 2017 to drive and measure industry progress to curb antimicrobial resistance. At least US$ 1.6 billion invested by its members into the development of AMR-relevant products to combat AMR in 2018, including 24 antibiotics and antifungals, 11 vaccines, 16 diagnostic platforms or assays, 10 non-traditional approaches, and one other AMR-relevant product.[22]
BEAM Alliance	Europe	BEAM (Biotech companies in Europe combating AntiMicrobial Resistance) Alliance is a strong network of approx. 65 small and medium-sized European companies involved in developing innovative products and kits to tackle AMR. In numbers, members of the BEAM Alliance together contribute over 120 potential new antibiotic compounds or curative and preventive technologies to this pipeline.[23]
CARB-X Combating Antibiotic-Resistant Bacteria	Global	CARB-X (Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator) is a global non-profit partnership dedicated to funding and supporting the early development of vaccines, diagnostics, antibiotics and other therapeutics that address the most serious drug-resistant bacteria. CARB-X is led by Boston University and funding is provided by BARDA, the Wellcome Trust, Germany's BMBF, the UK's Global Antimicrobial Resistance Innovation Fund (GAMRIF), the Bill & Melinda Gates Foundation, and with in-kind support from NIAID.[24]
imi innovative medicines initiative ND4BB TRANSLOCATION DRIVE AB RE-INVESTMENT IN R&D AND RESPONSIBLE ANTIBIOTIC USE	Europe	IMI is an EU public-private partnership funding health research and innovation (not unique to AMR). The IMI initiative ND4BB (New Drugs for Bad Bugs) represents an unprecedented partnership between industry, academia and biotech organisations to combat antimicrobial resistance in Europe. DRIVE-AB is a subsidiary program within the ND4BB which develops concrete recommendations for new economic models that would provide industry with an incentive to invest in this area while reconciling this with the need to use new antibiotics wisely.[25]
GARDP Global Antibiotic Research & Development Partnership	Global	The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit R&D organisation developing and delivering new or improved treatments for drug-resistant infections that pose the greatest risk to global health, while endeavouring to ensure their sustainable access.[26]
jpiamr Joint Programming Initiative on Antimicrobial Resistance	Global	In 2011, the European Commission established the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), together with 11 European member countries. Today, JPIAMR is a global collaborative platform and has engaged 27 nations to curb AMR with a One Health approach. The initiative coordinates national funding to support transnational research and activities within the six priority areas of the shared JPIAMR Strategic Research and Innovation Agenda – therapeutics, diagnostics, surveillance, transmission, environment and interventions.[27]
FIND Because diagnosis matters	Global	The Foundation for Innovative New Diagnostics (FIND) is a global not-for-profit organisation driving innovation in the development and delivery of diagnostics to combat major diseases, including drug-resistant bacterial infections. FIND is the diagnostics accelerator in the CARB-X global network.[28]

Of these research networks, CARB-X has the world's largest portfolio of early development pipeline products including new antibiotics, rapid diagnostics, vaccines and other life-saving products. CARB-X aims to accelerate global AMR innovation by encouraging and boosting early-stage development. It is investing up to US$500 million between 2016 and 2021 to support innovative antibiotics and other therapeutics, vaccines, and rapid diagnostics.[29] CARB-X has supported the establishment of accelerators in several countries. However, there is currently no CARB-X accelerator in Australia, and Australia at a national level is not recorded as a member of any of the above partnerships. A notable exception is FIND which has received funding from the Department of Foreign Affairs and Trade (through its Indo Pacific Centre for Health Security initiative) to support its diagnostic work.

Case study

The Community for Open Antimicrobial Drug Discovery (CO-ADD)

The Community for Open Antimicrobial Drug Discovery (CO-ADD – www.co-add.org), is a novel initiative launched by the University of Queensland in 2015 and funded for five years. It is a global open-access screening initiative to uncover significant and rich chemical diversity held outside of corporate screening collections. So far, they have screened over 300,000 compounds from more than 45 countries and 300 different academic groups. Researchers with positive results from initial screening can proceed with the development on this platform. This 'one-stop shop' helps fast track a novel compound from early stage research to identification of an investigational new drug candidate. CO-ADD has had multiple international funders and collaborators including the Wellcome Trust, GARDP and the PEW Trust and has recently launched a database for public access to the screening results.[30]

Although some Australian companies and researchers are collaborating with these groups, including the recently announced A$16 million international research deal between the University of Queensland's Institute for Molecular Bioscience and CARB-X[31], neither the scale nor the impact of these collaborations is sufficient to fully address identified gaps.

Case study

ARC Research Hub to Combat Antimicrobial Resistance

In 2019, the ARC Research Hub tackling antimicrobial resistance was established at the Kirby Institute with in total $8.8 million co-funded by the ARC and biotech companies and organisations. The hub aims to connect complex facets of antimicrobial resistance to develop new molecular diagnostic technologies and improve processes for new antibiotic identification. It has gathered an interdisciplinary collaboration of over 20 organisations from industry, research institutes, universities and hospitals/ clinics. Biotech companies such as SpeeDx Pty Ltd, Opal Biosciences, Boulos and Cooper and Cepheid, as well as NPS MedicineWise, GARDP and FIND have joined and co- funded the hub.[32]

4.3 Proposed Solutions

Australia has specific strengths in scientific research related to immunity and infectious diseases, as well as some unique pathogens of concern. An opportunity exists, consistent with objectives in the Australia's first National Antimicrobial Resistance (AMR) Strategy 2015–2019 and the recently released plan for 2020 and beyond, to develop a national research agenda for AMR. A detailed national AMR research agenda will guide long-term strategic target development over the next 5 to 10 years.

To support this research agenda, a coordinated whole-of-government approach through the new National Federation Reform Council (being established to replace Council of Australian Governments (COAG) meetings) and the National Cabinet Reform Committee on Health could facilitate coordinated, multi-jurisdictional efforts with a focus on AMR. Collaboration between various government departments could also broaden and deepen policy development. Expertise should be leveraged from different stakeholders including universities, research institutes, industry, professional healthcare groups, government and consumers to build a better 'eco-system' with coherent target prioritisation. A detailed national capability audit was agreed to be a critical next step to scope strengths and weakness and to pave the way for novel product development.

Development of a National AMR Research Agenda

- Whole-of-government approach
- Leveraged expertise from different stakeholders
- National capability audit

It was also agreed that establishment of an Australian AMR network involving key stakeholders from academia, government, industry, clinicians and consumer groups would form a solid platform to advance and tackle AMR issues. This new body would be well-placed to lead a comprehensive rethinking of models for antibiotic development and reimbursement and emphasise how Australia could complement and optimise its own national "push" and "pull" incentives. It would catalyse networks across academia, industry, clinicians and patients, thereby facilitating the exchange of information and resources to drive innovation to support development of new therapies, ensure Australia is linked in with global efforts, and drive activities to combat AMR.

Effective collaboration needs to be established between stakeholders with a fit-for-purpose framework to ensure better data sharing as well as resource integration and allocation.

Moreover, a comprehensive review and due diligence of regional and international partnerships is necessary to ensure alignment with Australia-specific priorities of AMR.

Establishment of an Australian AMR Network

- Active participation in and collaboration with international alliances
- Fit-for-purpose framework to ensure better data sharing as well as resource integration and allocation
- Facilitating the exchange of information and resources
- Recognition of the role of industry
- Review and due diligence of partnerships
- Education and advocacy

An AMR network as a single touchpoint would enhance Australia's ability to participate in and collaborate with international alliances. The established relationships between the Australian Government and other agencies (e.g. WHO) and countries (e.g. United Kingdom and the United States) could be leveraged for further AMR connections. Adaptation of international initiatives such as creating an accelerator like CARB-X in Australia should also be considered to boost the development of new antimicrobials.

Lastly, both education and communication of the significant threat posed by AMR should be boosted. The serious consequence of inaction on AMR could be promoted from a state level crossing different sectors to raise public awareness. Creation of an advocacy and education platform would address this lack of advocacy about AMR.

5 REGULATION OF ANTIMICROBIALS

Efforts to develop novel antimicrobials face challenges not only in terms of the science needing to be applied, but also in navigating regulatory processes and conducting clinical trials that are meaningful and efficient.

New antimicrobials do not easily fit within current clinical trial requirements in global approval pathways and a standardised set of outcomes by which they are assessed may diminish the comparative value of a novel treatment.

Moreover, while conducting non-inferiority trials is appealing at the practical and economic level, it is problematic for developers because the new product is likely to be compared against one or more genericised low-cost antimicrobials. As superiority has not been clinically demonstrated it is very difficult to achieve appropriate reimbursement that recognises the full societal value of these products. Demonstrating superiority is equally challenging due to the lack of a gold standard comparator in the setting of resistant organisms.

This is further compounded by patient selection. Many trials of novel antimicrobials have specific inclusion and exclusion criteria resulting in a trial population that does not reflect the larger real-world patient group which needs antibiotic treatment (e.g. focus on a few organ functions, eliminating patients above 65). Study requirements, comparators and patient recruitment all work against generating evidence that supports the wider value of novel antimicrobials.

Clinical Trial Requirements

- Lack of a standardised set of outcomes
- Patients not reflecting AMR patient profile
- Difficulty leveraging non-inferiority testing outcomes versus low cost generics
- Difficulty demonstrating superiority as lack of agreed gold standard comparators

5.1 Further Challenges: Australian Context

The Therapeutic Goods Administration (TGA) is responsible for ensuring that the medicines available in Australia are safe and efficacious. Specific TGA regulatory pathways already exist which can facilitate and/or accelerate patient access to prescription medicines. There are in total seven pathways (exhibited in Table 3) with one enabling access via personal importation of an overseas treatment (Special Access Scheme (SAS)).

Table 3: Regulatory Pathways in Australia

Regulatory Pathway	Description
Standard Pathway[33]	Standard pathway
Comparable Overseas Regulator (COR) A and B[34]	For medicines that received full overseas marketing approval following a de novo evaluation
Priority Review Pathway[35]	For addressing a life-threatening or seriously debilitating condition Substantial evidence needed demonstrating that the medicine provides a major therapeutic advance
Provisional Approval Pathway[36]	Time limited registration providing access to promising medicines where early availability outweighs risk of not having full dossier
Australia-Canada-Singapore-Switzerland (ACSS) Work Sharing Pathway (pilot program)[37]	Faster approval potentially via work sharing with ACSS participating regulators
Orphan Drug Designation Pathway[38]	One indication, serious condition (life threatening/debilitating), medical plausibility, prevalence thresholds, financial viability and no other ARTG goods could reasonably be used Must not have been previously refused for approval on safety grounds *Note that Australia only offers a "fee waiver" (no registration and PBAC submission fees) within this pathway, whereas market exclusivity and/or subsidies towards the cost of clinical trials and regulatory assistance are offered in other jurisdictions*
Special Access Scheme (SAS)[39]	For access to unapproved medicines or medicines that are discontinued/are in shortage (under exceptional clinical circumstances) Costs to hospitals as no option for PBS

These frameworks do not all apply to novel antimicrobials. Orphan designation is intended to provide an incentive for the registration of medicines for small populations (by virtue of fee waiver), and is appropriate for some novel antimicrobials. The provisional and priority review pathways, however, are not tailored for novel antimicrobials, particularly as they require demonstrated superior efficacy in clinical trials and do not have a unique treatment target. Australians currently have limited access to novel antimicrobials, mainly via clinical trials and the SAS.

Notably, there have only been two antibiotic approvals in the last few years with bacteriophages or other novel antimicrobials not being amongst them.

Repurposing existing medicines may serve as a new strategy in the fight against AMR. However, the process for broadening indications of existing drugs for on-label use has been reported to be onerous and repurposing efforts are understood to be limited by the hurdles and cost of updating dossiers to the latest standards. In addition, balancing industry and regulator needs was seen as challenging during marketing authorisation processes.

Case study

Repurposing of Existing Medicines

Prof. Mark Walker from the University of Queensland has identified a metal transport drug PBT2 as a promising therapeutic against antibiotic resistant bacteria[40]. Initially developed for the treatment of Alzheimer's and Huntington's diseases, PBT2 was found to be well tolerated by humans in previous clinical trials[41,42]. Disrupting metal content can induce toxicity in bacteria and PBT2 indicated capacity to break multiple classes of bacterial antibiotic resistance and fight infectious diseases. This repurposing work is a novel, potentially cheaper strategy to expeditiously populate the AMR pipeline. However, several hurdles exist for its successful implementation, including patent harmonisation for composition and method, patent lifetime issues, availability of previous safety data and funding challenges. Among them, the bridging funding for development of the repurposed drug remains a major roadblock. As the patents of many of these medicines have expired or are nearing the end of their lifetime, there is a lack of interest from big pharma to fund the clinical trials.

Therefore, while the Australian general regulatory framework has evolved and now includes multiple pathways to regulatory approval, there continue to be issues faced by antimicrobial developers.

There is a significant cost to marketing a new prescription medicine which includes submitting a marketing authorisation application and post marketing authorisation commitments. Collectively, these can be prohibitive for smaller manufacturers, either in Australia or elsewhere around the world. Companies developing innovative new antimicrobials for which there is no standard regulatory pathway may face even higher costs which can limit both new entrants in the Australian AMR sector and the range of generic antimicrobials.

Challenges relating to companion diagnostics also contribute to the difficulties that novel antimicrobials face in Australia. Diagnostic technologies are required to undergo registration each time a new test is added to the platform, incurring the full cost of registration.

Regulatory Barriers

- Disqualification of antimicrobials from many regulatory pathways
- Difficulty and cost of repurposing
- Cost of regulatory review
- Difficulty interfacing with the regulator
- Potential short window of market exclusivity
- Regulatory barriers for diagnostics

For the new antimicrobials that make it to the market, regulatory challenges continue, including the relatively short window between establishment of intellectual property rights and generic production (compared to the European Union member countries). Australia allows for 5 years of regulatory data protection (data exclusivity) for new pharmaceuticals[43] whereas European Union countries allow for 10 years[44], protecting the originator company's data for longer. This requires low cost generic manufacturers to generate their own clinical dataset or to wait until the end of the data exclusivity period so as to be able to use the originator company's data, thereby potentially delaying their market entry.

Combined with the challenges in achieving prices that reflect the full value of the product (see next section), this shorter period of data exclusivity may limit the return on investment for developers, and may discourage future R&D and commercialisation efforts.

Additionally, it is understood that there is no established mechanism for reviewing off-label usage of antimicrobials, which may mean that a large amount of off-label antibiotic use is not recorded.

Lifespans of new antimicrobials are further limited by their expiry dates, more so than most pharmaceuticals. Standard procurement practice in Australia requires a minimum of six months residual shelf life which not only limits the use of products technically still meeting quality standards, but is also believed to be causing large amounts of waste due to unrealised potential. This is exacerbated for antimicrobials and AMR because of the tendency to reserve some products, thus creating stockpiles that readily reach expiry date. This is understood to be contributing to the supply shortages which plays a highly critical role in addressing a public health concern.

Supply Issues

- Supply shortages and waste due to current procurement processes requiring six months of shelf life
- Supply issues caused by SAS timeframes and long supply chains

In addition, the SAS, through which some novel antimicrobials are currently supplied carries the risk of not being able to adequately respond to potential crisis issues. Supply times from overseas can be long and may limit responsiveness if a crisis occurs.

5.2 What is Done Internationally?

Several regulatory approaches in jurisdictions outside Australia have facilitated commercialisation of novel antimicrobials (shown in Table 4 below).

Table 4: Regulatory Pathways (Overseas)

Pathway	Description
The Generating Antibiotics Incentives Now (GAIN) Act[45]	A US bill ratified in 2012, which provides five years of additional market exclusivity for those new antibiotics designated under the law as a "qualified infectious disease product," (defined as "an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections"), along with priority review and fast track approval *The FDA guidance for antibiotic development (including clinical trials guidance)*
Priority review vouchers[46]	US legislation enacted in 2007 to provide an incentive to develop drugs for neglected tropical diseases by allowing the FDA to grant companies that obtain approval for a drug for a tropical disease a one-time, transferable priority review voucher for an unrelated future drug. These vouchers could facilitate faster patient access to antibiotics and the possibility for voucher application to blockbuster drugs draws large cap companies to antibiotic market
Orphan drug designations[47]	Special drug designation status offered by FDA and EMA – historically effective at stimulating R&D of drugs with poor reimbursement prospects. Benefits include extended market exclusivity, subsidies towards the cost of clinical trials and assistance to manufacturers navigating through regulatory requirements
Limited Population Antibacterial Drug (LPAD)[48]	The FDA LPAD pathway facilitates the development and approval of certain antibacterial and antifungal drugs to treat serious or life-threatening infections in limited populations of patients with unmet needs. The development programs for drugs eligible for approval under the LPAD pathway follow streamlined approaches to clinical development. This may involve smaller, shorter or fewer clinical trials

5.3. Proposed Solutions

In recent years the Australian regulatory environment has seen a number of positive developments, especially with regard to the approval of medicines and embracing new pathways.

Further novel regulatory pathways and incentives are required for the development of new and emerging antimicrobial technologies and to facilitate the regulation and registration of novel antimicrobials.

There is also a push for international harmonisation of regulatory pathways, and Australia is already benefiting from international collaboration in areas such as oncology. Australia should review examples and best practices implemented in the global context, and reflect on how these pathways could be adapted here, or how existing pathways could be adapted to better serve the mission of bringing new antimicrobials to market.

Regulatory Incentives

- Additional market exclusivity or additional data exclusivity
- Waiving of registration fees
- Facilitation of repurposing of existing drugs
- Facilitation and expedition of the regulation of companion diagnostics

An appropriate regulatory pathway for repurposing would allow for a simpler and less expensive scheme for existing medicines that may have efficacy against resistant organisms. Regulation of companion diagnostics should also be facilitated and expedited.

AMR-Specific Streamlined Pathways

- Orphan drug category be adapted to allow for antimicrobials to be considered
- Fast track process specifically for antimicrobials/ priority review vouchers

Streamlined regulatory approaches made specific to AMR may allow for faster development, expedited review and earlier access for patients. Options for a regulatory scheme suitable for novel antimicrobials (e.g. bacteriophages) could include adapting the existing orphan drug designation, and a fast track process specifically for antimicrobials. The option of a priority review voucher approach was also widely discussed by workshop participants.

Additional regulatory incentives could be used, either to support these new pathways, or as standalone incentives. These could include stronger market or data exclusivity provisions, registration fee waivers (which could improve the cost structure for small businesses) and facilitation of existing drug repurposing for their indications to be expanded (i.e. making exceptions to necessary supporting data based on safety history).

Review of Trial Requirements

- Clinical trial design
- Patient enrolment
- Levels of data to support approvals
- Indications

Further review of clinical trial requirements may also support faster access to new antimicrobials. The assessment process should be tailored to reflect understanding of the differences between treating communicable and non-communicable diseases. This may require different approaches to determining the most appropriate trial endpoints to support value for both the patient and public health system.

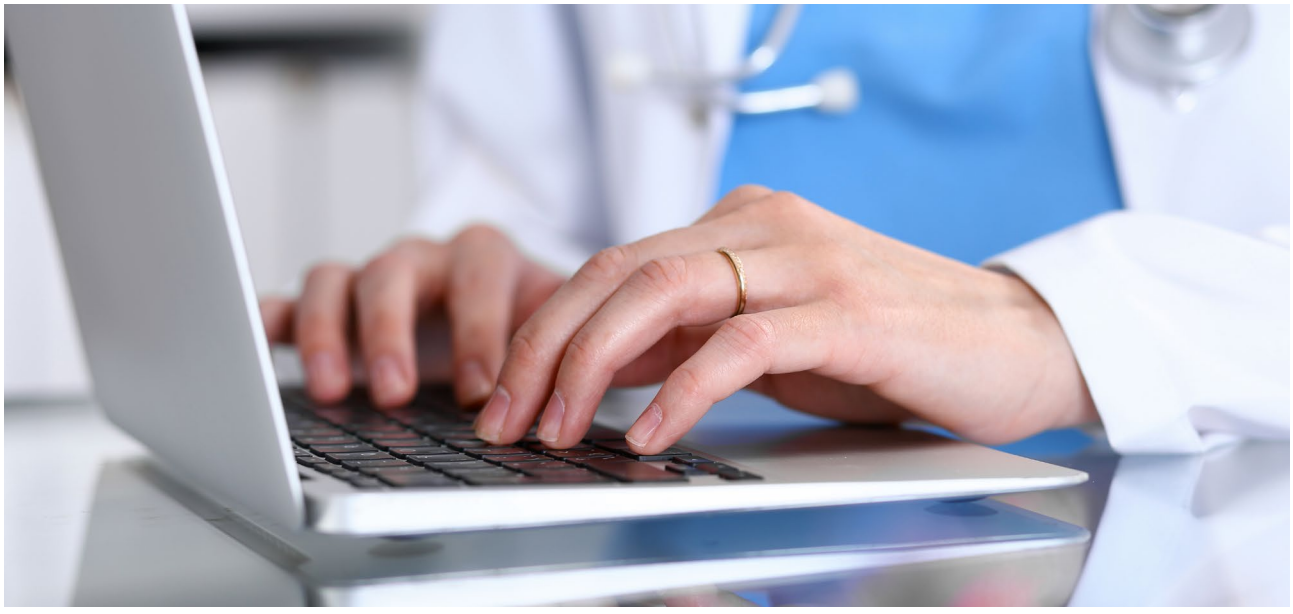
Therefore, various aspects of the clinical requirements for registration could be adapted to better suit novel antimicrobials and there is an opportunity for Australia to be a pioneer in addressing this problem, faced by many countries.

Workshop participants suggested a range of options to improve four aspects of clinical trials: Clinical trial design, Patient enrolment, Levels of data to support approvals, and Indications, displayed in Table 5.

Table 5: Suggested Changes to Clinical Trials

Suggested changes	Description
Clinical trial design	Improving the way efficacy is tested by establishing a standardised set of outcomes for antimicrobial trials
Patient enrolment	Stratification of patients to provide improved regulatory evidence
Levels of data to support approvals	Eliminating some phases of trials where data already collected is adequate to support treatment of patients, given the fact that therapeutic drug monitoring will be ongoing (i.e. efficacy to be proven at the actual treatment stage with PK-PD conducted with volunteers at trial stage). Reliance on safety data to support regulatory approval of repurposed medicines. Acceptance of a lower efficacy level (proven in the trial) in the presence of a TGA-approved real-time companion diagnostic to detect the resistance of the organism
Indications	Seeking regulatory approval on the basis that the targeted bacteria becomes the indication, instead of the site of infection (e.g. UTI) being the indication.

These approaches would ideally be supported by improved post-marketing surveillance, in particular for new fast-tracked antimicrobials.



6 PRICING, REIMBURSEMENT AND SUPPLY CHAIN

Securing a sustainable supply of essential antimicrobial products, as well as affordable access to novel therapies is crucial to address the growing threat of AMR. However, market conditions globally remain challenging and are not designed to provide reward for the investment involved.

Novel antimicrobials are usually undervalued by current HTA processes, creating a disincentive for companies to conduct antimicrobial R&D. Current pricing models also do not recognise the full value of these products. Even if value-based pricing principles are applied, the associated HTA and economic evaluation do not consider all relevant dimensions of value. Novel antimicrobials are relatively low cost compared with treatments for other disease areas such as oncology, where HTA and payers are more likely to recognise the value of addressing unmet clinical need.

Moreover, prices do not reflect the fact that sales volumes of novel antimicrobials are likely to be limited by short treatment duration and that stewardship programs to ensure their judicious use dictate they will likely be reserved for highly resistant infections.

Current HTA systems (especially those employing cost-effectiveness analysis) do not work well for novel antimicrobial therapies.

Current Pricing Models and HTA Systems Unable to Deliver Adequate Market Reward

- Prices do not reflect the value represented by products
- Prices do not reflect sales volumes and are likely to be limited by the short treatment duration and being reserved for highly resistant infections (low demand)
- Novel antimicrobials are likely to be compared to low-cost generics within the HTA process

Firstly, they are likely to be compared to low-cost generics. This makes it very unlikely that the novel agents will be able to demonstrate acceptable levels of superiority to deliver expected cost-effectiveness.

Secondly, current HTA systems focus mainly on patient-relevant clinical outcomes as reported in clinical trials and do not capture the full range of benefits for patients, institutions and society. This includes the insurance value associated with simply having these options available (in the event of outbreaks of resistant organisms).

6.1 Further Challenges: Australian Context

In Australia, the traditional HTA assessment process leading to reimbursement via the Pharmaceutical Benefits Scheme (PBS) is based on assessment of comparative effectiveness and cost-effectiveness (similar to several other jurisdictions including the United Kingdom). As mentioned above, this type of assessment and current pricing and payment models (per unit prescription) undervalues novel antimicrobials, comparing them to the low-cost (often generic) comparators and not accounting for their broader, long-term value to patients with drug-resistant infections, health systems and to society as a whole.

Current procurement policies in Australia also do not suit all antimicrobials.

Public hospitals are funded via state health budgets, and funding constraints further limit the use of novel antimicrobials, as the pharmaceutical component of a hospitalisation may be incorporated into a bundled payment (such as a Diagnostic Related Category) and generics represent a cheaper therapeutic option. This inability to achieve appropriate prices further disincentivises companies developing novel antimicrobials to stay in the market and in turn, can create shortage issues.

Complex Procurement Policies

- Hospital budget constraints further limit antibiotic use and disincentivises existing and new antibiotic developers
- Good stewardship is difficult
- Significant gaps remain in identifying how hospitals prescribe antimicrobials and how these medicines are being used in wider community

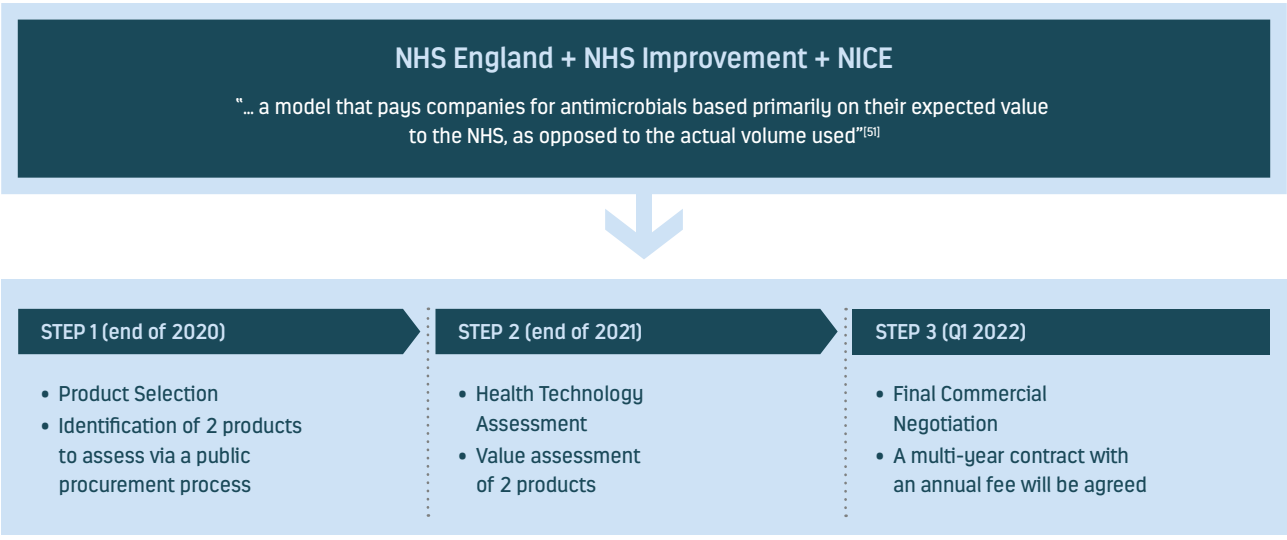
Moreover, the relatively low value placed on antimicrobials, the tendency to default to lower cost older products and the movement of patients between institutions make good stewardship difficult. Significant gaps remain in understanding how hospitals utilise the full range of antimicrobials and how these medicines are being used in wider community.

6.2 What is Done Internationally?

The UK is a pioneer in developing an innovative model for the evaluation and purchase of antimicrobials. The National Health Service (NHS) UK and National Institute for Health and Care Excellence (NICE) recognised that novel antibiotics need to be treated differently in both HTA and procurement processes. This has led to the joint development of a national health plan to develop a model that pays primarily on the overall expected value of a novel antimicrobial to the NHS, as opposed to the actual volume used. Within this model, payments to companies are de-linked from volume of antibiotics sold, supporting the value-based assessment of medicines (more akin to using a 'subscription' model). Under the program, the NHS will pay companies up front for access to effective novel antibiotics[49,50].

The NHS and NICE recognise that the starting point in this reform is to modify the existing HTA process to ensure the appropriate dimensions of value are incorporated into the assessment. Making these changes (and developing an HTA process specific to novel antimicrobials) requires extensive stakeholder consultation and is likely to include additional steps within a modified process. For example, greater recognition of economic models of transmission effects and increased use of expert opinion to assist in estimating the insurance and societal value (which is likely to vary by the type of resistant organisms and infection settings). NICE has also recognised the need to understand health system and institutional costs and values, for example those associated with avoiding closures of operating theatres or hospital wards in the event of uncontrolled outbreaks of resistant organisms. The collaboration between NICE and the NHS also recognises that the challenges don't finish with a modified HTA approach. Actual procurement and pricing processes that build on the wider assessment of value will also be required. This led to a pilot with the expectation that it will take at least two years before outcomes from this new approach can be assessed.

Diagram 1: NICE & NHS' New HTA Framework



Learnings will be shared with other jurisdictions to assist them to develop similar models, however, it would be prudent for Australia to begin working on modifying its HTA and procurement systems earlier, rather than wait for several years to learn the outcomes of the pilot.

6.3 Proposed Solutions

Workshop participants acknowledged that pricing and HTA reform is needed to better capture the full value of antimicrobials in the HTA process and to provide incentives for continued private sector investment in antimicrobial R&D.

Without these incentives, the burden of developing new antimicrobial therapies falls on governments, who are currently not appropriately resourced to undertake such a task. This has been recently explored in various reports from the Office of Health Economics and DRIVE-AB. These reports advocate for the development of a new type of value assessment model[52].

Workshop participants suggested these developments should be closely followed and learning applied in Australia but expressed concern regarding the time it will take to see outcomes from these pilots. An assessment process should include additional dimensions of value for novel antimicrobials, to include wider public health benefits – the value of limiting the spread of infections to the wider population, ensuring that treatments will be available for future critical health problems, the value of offering more options for infections to preserve the efficacy of existing therapies, and the overall value of having novel mechanisms of action for drug-resistant infections. However, broadening the values being assessed is technically complex and likely to be slow. Moreover, to address the issue of pricing not reflecting value, it was suggested that certain price incentives may need to be considered, including price premiums over low cost generics, add-on payments or the setting of a minimum price level to provide 'affirmative action'. This strategy could reflect antimicrobials being valued more highly by society, consequently leading to increased market rewards and incentives, and potentially also offering a solution to supply shortages.

Pricing and HTA Reform

- Inclusion of additional values of novel antimicrobials for wider health benefits
- Price premiums over low cost generics
- Setting of a minimum price level to increase the pricing bar
- PBS list price to be automatically readjusted when there is sole supply

Another practical solution suggested to address shortages was to automatically readjust the PBS list price when there is sole supplier to cover the costs of keeping the product viable for the sponsor company and provide continuity of supply.

Moreover, new reimbursement models and ways of purchasing antimicrobials are necessary. Alternative payment schemes could be implemented to incentivise new antimicrobials to enter the Australian market. The UK's proposed "subscription" style model, in which the payments made to companies are de-linked from the volumes of antibiotics sold, should be closely monitored and evaluated, and a similar model adopted or piloted in Australia. Australia has a real opportunity to show global leadership in AMR policy, as has been demonstrated with Hepatitis C treatments.

Case study

'Netflix' Model for Hepatitis C in Australia

Australia instituted a novel procurement model in 2015, agreeing to spend about AU$1 billion to treat an estimated 104,000 Hepatitis C patients over five years. This included negotiating prices with several manufacturers[53]. A recent analysis published by the New England Journal of Medicine estimated that Australia would save by using this method instead of the traditional reimbursement method[54]. The Kirby Institute reported that there was a more than tenfold increase on the number of people treated per year during the decade prior to the new program[55]. While this has been an effective strategy to combat an infectious disease, it also guaranteed an income for the manufacturers, regardless of the amount of product sold. England is now working towards similarly novel agreements for antimicrobials where NICE and NHS are calling for companies to identify products to be considered for the pilot test[56].

Other reimbursement reforms suggested included accelerated PBAC review and special provisions/exemptions for particular pathogens. Questions were raised as to the most appropriate reimbursement mechanism. For example, the possibility of listing under a formulary different to the PBS (i.e. creation of a new formulary solely for antibiotics) to streamline the review process and realise the value and potential of novel antimicrobials. However, given the legislative restriction on the PBAC (a remit to make recommendations only regarding listing on the PBS), this raises wider considerations. A funding mechanism other than the PBS may be appropriate, which would then require the HTA component to be conducted by another body such as the Medical Services Assessment Committee (MSAC).

New Reimbursement and Procurement Models

- Alternative payment schemes including models where payments are de-linked from sales volume
- Accelerated PBAC review
- Special provisions/exemptions for particular challenging pathogens
- Listing new antimicrobials under a different formulary
- Diagnostic reimbursement incentives
- Reimbursement pathway to differ depending on setting

A diagnostic reimbursement incentive was also suggested such that, if companion diagnostics are required, a co-dependent application via MSAC could be incentivised.

To address the shortage and undervaluation issue associated with both the current HTA process and the nature of hospital funding, the reimbursement pathway could differ depending on the setting (community vs. hospital).

A suggestion was also made around the creation of a separate Commonwealth insurance fund for novel antimicrobials, which could be used when needed.

Better Data Collection and Collaboration

- Comprehensive information on usage, epidemiology and patient outcomes to be collected
- Industry to participate in initiatives related to stewardship and optimal prescribing
- Ongoing collaboration among different stakeholders

Finally, the importance of better data collection and collaboration were highlighted to demonstrate the value of antimicrobials. Comprehensive information should be collected on antimicrobial usage, epidemiology and patient outcomes.

This information could provide insight into the re-evaluation of the cost-effectiveness of these medicines to better show value.

Industry may have broader access to utilisation data sets and should therefore be included in initiatives related to antimicrobial stewardship and promotion of optimal antimicrobial prescribing.

Ongoing collaboration among different stakeholders across the full antimicrobial value chain is necessary to ensure not only appropriate value is being placed on antimicrobials, but also to ensure their secure supply by providing increased traceability and transparency.

7 CONCLUSION

This was the first multi-stakeholder workshop on this urgent public health issue that focused exclusively on product development gaps.

There was a high degree of engagement and support from participants from the public and private sectors, who among other things agreed that the workshop should not be a stand-alone event, but the start of an ongoing forum.

MTPConnect looks forward to continuing the dialogue and enhancing collaboration across both the public and private sectors to support the development of new technologies to tackle AMR, one of the most serious threats to humanity, with an urgent call to action.

8 REFERENCES

[1] Review on Antimicrobial Resistance: Tackling drug-resistant infections globally. The Review on Antimicrobial Resistance Chaired by Jim O'Neill. (2014). https://amr- review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1. pdf

[2] Interagency Coordination Group on Antimicrobial Resistance. (2019) No Time to Wait: Securing the Future from Drug- Resistant Infections: Report to the Secretary-General of the United Nations. https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_final_report_EN.pdf?ua=1

[3] Zhou F, Yu T, Du R et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395: 1054-1062

[4] World Health Organization. (2019). 2019 Antibacterial Agents in Clinical Development. https://apps.who.int/iris/bitstream/handle/10665/330420/9789240000193-eng.pdf

[5] Australian Government Department of Health. Public Consultation on Australia's Next Antimicrobial Resistance Strategy 2020 and Beyond. (2019). https://consultations.health.gov.au/ohpd-health-protection-policy-branch/consultation-on-next-amr-strategy/

[6] Australian Government. Australia's National Antimicrobial Resistance Strategy – 2020 and Beyond. https://www.amr.gov.au/news/australias-national-antimicrobial-resistance-strategy-2020-and-beyond

[7] Australian Government. Antimicrobial Resistance: Objective 5: Research and development (2017). https://www.amr.gov.au/australias-response/objective-5-research-and-development

[8] NPS MedicineWise (2016). Antibiotic resistance in Australia: here and now. https://www.nps.org.au/news/antibiotic-resistance-in-australia-here-and-now#r6

[9] op cit. Zhou et al

[10] Centers for Disease Control and Prevention (2009). Bacterial co-infection in lung tissue specimens from fatal cases of 2009 pandemic influenza A (H1N1) – United States, May-August 2009. Morb. Mortal. Wkly. Rep. 58 1071–1074

[11] Morens DM, Taubenberger JK, Fauci AS (2008). Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2599911/

[12] International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC). COVID-19 Report: 19 May 2020. https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_ Platform_COVID-19_Report_19MAY20.pdf

[13] Renwick M.J. et al. (2016). Targeting innovation in antibiotic drug discovery and development. https://www.euro.who.int/__data/assets/pdf_file/0003/315309/Targeting-innovation-antibiotic-drug-d-and-d-2016.pdf

[14] The PEW Charitable Trusts. A Scientific Roadmap for Antibiotic Discovery (2016). https://www.pewtrusts.org/~/media/assets/2016/05/ascientificroadmapforantibioticdiscover y.pdf

[15] Renwick M. & Mossialos E. (2018): What are the economic barriers of antibiotic R&D and how can we overcome them? Expert Opinion on Drug Discovery, 13:10, 889-892, DOI: 10.1080/17460441.2018.1515908

[16] ibid

[17] G20 (2017), 'G20 Leaders' Declaration. Shaping an interconnected world'. http://www.oecd.org/els/health-systems/G20-leaders-declaration.pdf

[18] The New York Times (2019). Deadly GERMS, Lost Cures: Crisis Looms in Antibiotics as Drug Makers Go Bankrupt. https://www.nytimes.com/2019/12/25/health/antibiotics-new- resistance.html

[19] Provided courtesy of NHMRC secretariat

[20] Australian Commission on safety and Quality in Health Care. AURA 2019. Third Australian report on antimicrobial use and resistance in human health (2019). https://www.safetyandquality.gov.au/sites/default/files/2019-06/AURA-2019-Report.pdf

[21] GLOPID-R. About us: Members. https://www.glopid-r.org/about-us/members/. Accessed December 2019

[22] AMR industry alliance. 2020 Progress Report, January 2020. https://www.amrindustryalliance.org/wp-content/uploads/2020/01/AMR-2020-Progress-Report.pdf

[23] BEAM Alliance. Biotech companies from Europe innovating in anti-microbial resistance research (2019). https://beam-alliance.eu/wp-content/uploads/2019/10/2019-10-beam- leaflet-v1-0.pdf

[24] About CARB-X – Overview. https://carb-x.org/about/overview

[25] Innovative medicines initiative. ND4BB new drugs for bad bugs (2017). https://www.imi.europa.eu/sites/default/files/uploads/documents/projects/IMI_AMR_2017_ LR.pdf

[26] Global Antibiotic Research & Development Partnership. About GARDP. https://www.gardp.org/about/. Accessed December 2019

[27] Joint Programming Initiative on Antimicrobial Resistance. About JPIAMR. https://www.jpiamr.eu/about/. Accessed December 2019

[28] Foundation for Innovative New Diagnostics. At a glance. https://www.finddx.org/at-a-glance/

[29] op cit. CARB-X

[30] Zuegg et al. How to Stimulate and Facilitate Early Stage Antibiotic Discovery ACS Infect. Dis. 2020, 6, 1302–1304 https://pubs.acs.org/doi/pdf/10.1021/acsinfecdis.0c00163

[31] Superbug drug discoveries spark gobal deal. 23 June 2020. https://imb.uq.edu.au/article/2020/05/superbug-drug-discoveries-spark-global-deal

[32] Kirby Institute. ARC awards $5m to establish research hub tackling antimicrobial resistance at the Kirby Institute. https://kirby.unsw.edu.au/news/arc-awards-5m-establish- research-hub-tackling-antimicrobial-resistance-kirby-institute. Accessed December 2019

[33] Department of Health, Therapeutic Goods Administration: Prescription medicines registration process. https://www.tga.gov.au/prescription-medicines-registration-process. Accessed December 2019

[34] Department of Health, Therapeutic Goods Administration: Comparable overseas regulators (CORs) for prescription medicines. https://www.tga.gov.au/publication/comparable-overseas-regulators-cors-prescription- medicines. Accessed December 2019

8 REFERENCES

[35] Department of Health, Therapeutic Goods Administration: Priority review pathway: prescription medicines. https://www.tga.gov.au/priority-review-pathway-prescription- medicines. Accessed December 2019

[36] Department of Health, Therapeutic Goods Administration: Provisional approval pathway: prescription medicines. https://www.tga.gov.au/provisional-approval-pathway-prescription-medicines. Accessed December 2019

[37] Department of Health, Therapeutic Goods Administration: ACCS – NAS work sharing initiative. https://www.tga.gov.au/acss-nas-work-sharing-initiative. Accessed December 2019

[38] Department of Health, Therapeutic Goods Administration: Orphan drug designation. https://www.tga.gov.au/publication/orphan-drug-designation. Accessed December 2019

[39] Department of Health, Therapeutic Goods Administration: Special access scheme. https://www.tga.gov.au/form/special-access-scheme. Accessed December 2019

[40] Bohlmann L, DeOliveira DMP, et al. (2018). Chemical synergy between ionophore PBT2 and zinc reverses antibiotic resistance. mBio. 9(6). Pii: e02391-18

[41] Lannfelt L, Blennow K, et al. (2008). Safety, efficacy, and biomarker findings of PBT2 in targeting Abeta as a modifying therapy for Alzheimer's disease: a phase IIa, double-blind, randomised, placebo-controlled trial. Lancet Neurol. 7(9): 779-86

[42] Huntington Study Group Reach2HD Investigators. (2015). Safety, tolerability, and efficacy of PBT2 in Huntington's disease: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet Neurol. 14(1): 39-47

[43] Parliament of Australia. Parliamentary Business. Chapter 4 – Pharmaceuticals and Health. https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Former_Committees/f reetrade/report/final/ch04. Accessed December 2019

[44] European Medicines Agency. Data exclusivity, market protection, orphan and paediatric rewards (2018). https://www.ema.europa.eu/en/documents/presentation/presentation- data-exclusivity-market-protection-orphan-paediatric-rewards-s-ribeiro_en.pdf

[45] PEW. GAIN: How a New Law is Stimulating the Development of Antibiotics (2013). https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2013/11/07/gain-how-a- new-law-is-stimulating-the-development-of-antibiotics

[46] Renwick M.J. et al (2016): A systematic review and critical assessment of incentive strategies for discovery and development of novel antibiotics; The Journal of antibiotics 69, 73-88, doi:10.1038/ja.2015.98

[47] ibid

[48] US Food and Drug Administration (FDA): Limited Population Pathway for Antibacterial and Antifungal Drugs – the LPAD Pathway. https://www.fda.gov/drugs/development- resources/limited-population-pathway-antibacterial-and-antifungal-drugs-lpad-pathway. Accessed December 2019

[49] NICE (2019). https://www.nice.org.uk/Media/Default/About/what-we-do/NICE- guidance/antimicrobial guidance/AMR-launch-statement.docx

[50] CIDRAP, University of Minnesota, CIDRAP. News & Perspective. UK to test new payment model for antibiotics (2019). http://www.cidrap.umn.edu/news-perspective/2019/07/uk- test-new-payment-model-antibiotics

[51] Grover, N. (2019). UK courts antibiotic developers with 'subscription-style' incentive to combat superbug scourge. https://endpts.com/uk-courts-antibiotic-developers-with-subscription-style-incentive-to-combat-superbug-scourge/

[52] IFPMA AMR Policy Position: Reimbursement and Health Technology Assessment reform (2018). https://www.ifpma.org/wpcontent/uploads/2018/09/IFPMA_AMR_Position_Incentives_HTA_Reimbursement_2018.pdf

[53] PEW. A Netflix Model for Hepatitis C: One Price, Unlimited Meds (2019). https://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2019/02/25/a-netflix- model-for-hepatitis-c-one-price-unlimited-meds

[54] Moon S. (2019). Universal Medicine Access through Lump-Sum Remuneration – Australia's Approach to Hepatitis C. NEJM. 380: 607-610

[55] The Kirby Institute. News. From chronic to cured: could Australia be the first country in the world to eliminate hep C? (2019). https://kirby.unsw.edu.au/news/chronic-cured-could- australia-be-first-country-world-eliminate-hep-c

[56] GOV.UK News story: Development of new antibiotics encouraged with new pharmaceutical payment system. https://www.gov.uk/government/news/development-of- new-antibiotics-encouraged-with-new-pharmaceutical-payment-system. Accessed December 2019

9 APPENDIX

9.1 List of Workshop

Name	Organisation	Role
Adrian Bootes	Therapeutic Goods Administration	Assistant Secretary, Head of Prescription Medicines Authorisation Branch
Alan Liddle	Haemalogix	Non-Executive Director
Andrew Bowskill	MTPConnect	Director of Stakeholder Engagement for Queensland
Andrew Mosley	Ausbiotech	Director, Policy and Programmes
Anne-Maree Englund	MSD	Policy Manager
Bernard Hudson	Royal North Shore Hospital	Infectious Diseases Specialist
Betsy Anderson-Smith	Medicines Australia	Policy Officer
Branwen Morgan	University of Technology Sydney	Managing Director and Co-founder of OUTBREAK
Brendan Allen	Burnet Institute	Executive General Manager, Business Development and Funding Partnerships
Brendan Murphy	Department of Health	Australian Government Chief Medical Officer
Chris Archer	TAS Health	Senior Specialist Pharmacist, Medication Strategy and Reform
Cindy Toms	Department of Health	Director of the Antimicrobial Resistance Section, Office of Health Protection
Colin Denver	SpeeDx	Chief Executive Officer
Daniel Grant	MTPConnect	Managing Director and Chief Executive Officer
David Abbott	Department of Health	Principal Research Scientist, Health and Medical Research Office
David Grainger	Biointelect	Head, Global Health Outcomes and Policy
David Grolman	Pfizer	Medical Director
Deniz Morali	Biointelect	Associate
Donna Mak	WA Health	Senior Medical Advisor, Communicable Disease Control Directorate
Felicia Pradera	DMTC	Medical Countermeasures Program Leader
Helen Critchley	Sanofi	Global Regulatory Affairs Country Head ANZ
Jane Ryan	University of Technology Sydney iThree Institute	Chair of the Advisory Board
Jennifer Herz	Biointelect	Managing Director
John Turnidge	Australian Commission on Safety and Quality in Health Care (ACSQHC)	AMR and Antibiotic Usage Program Leader
Judith Mitchell	Next Science	Managing Director
Julie Phillips	BioDiem	Executive Director and Chief Executive Officer
Justin Lee	QLD Health	Director, Medication Services Queensland
Karin Thursky	National Centre for Antimicrobial Stewardship (NCAS)	Director

9 APPENDIX

Name	Organisation	Role
Karlee Johnston	ANU Medical School	Chair, SHPA Critical Care Leadership Committee
Kenneth Hargreaves	MSD	Associate Medical Director, Specialty Care
Kent Garrett	Austin Health	Director of Pharmacy
Lauren Adler	Pfizer	General Manager and Director, Essential Health
Lee Davelaar	Pfizer	Strategic Policy Manager
Louise Clarke	Department of Health	Assistant Secretary, Office of Health Technology Assessment – Policy
Louise Flood	SA Health	Program Coordinator
Mark Blaskovich	Community for Open Antimicrobial Drug Discovery (CO-ADD)	Program Coordinator
Mark Walker	University of Queensland	Director, Australian Infectious Diseases Research Centre
Max Liddle	Biointelect	Associate
Michael Song	Department of Industry	Senior Policy Officer, Commercialisation Policy Branch
Paul Field	GARDP and FIND	Australian Representative
Philip Siew	Roche Diagnostics	Molecular Systems Business Development Manager
Ramiz Boulos	Boulos & Cooper	Founder, Director & Chief Executive Officer
Rebecca Guy	University of New South Wales Kirby Institute	Leader, ARC Research Hub to Combat AMR
Rob Grenfell	Commonwealth Scientific and Industrial Research Organisation (CSIRO)	Director, Health and Biosecurity Business Unit
Sarah Norris	Department of Health	Assistant Secretary, Health Protection Policy
Tania Sorrell	NHMRC Centre of Research Excellence in Emerging Infectious Diseases (CREID)	Director, Marie Bashir Institute for Infectious Diseases and Biosecurity
Tanya Applegate	University of New South Wales Kirby Institute	Senior Lecturer, Viral Hepatitis and Clinical Research Program
Tim Cogin	MSD	Business Unit Manager
Tina Cheng	Biointelect	Associate
Vicki Gardiner	Medicines Australia	Director of Policy & Research

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Further information about the Industry Growth Centres Initiative is available at www.business.gov.au/industrygrowthcentres