

Australian Government
Department of Health
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Re: Australia's Antimicrobial Resistance Strategy – 2020 and beyond

Medicines Australia welcomes the opportunity to respond to the Australian Government Department of Health consultation on Australia's Antimicrobial Resistance Strategy – 2020 and beyond.

Medicines Australia is the peak industry body representing the research-based medicines industry in Australia: Innovative companies that research, develop, manufacture and supply new medicines and vaccines to the Australian market. Our members are proud of the contribution they make to the health and well-being of everyday Australians, as well as to the local economy. Our industry provides high value jobs for Australians, generates up to \$4 billion in exports and invests over \$1 billion in research and development every year¹.

Introduction

The discovery of antimicrobials and their development to treat bacterial infections was one of the most important achievements of the 20th Century. Since antimicrobials were first commercially produced, initially for use in human medicine and subsequently in veterinary medicine and agriculture, their use has been associated with the risk of emergence of antimicrobial resistance (AMR). At the same time as the world has observed accelerated emergence of resistance, companies are pulling out of antibiotic research and fewer new antibiotics are being approved. Today AMR is recognized as one of the world's most pressing global health priorities. New antimicrobial drugs are urgently needed to address the growing threat of AMR.

Medicines Australia believes that market-based mechanisms represent the most efficient way to sustainably incentivize investment in antimicrobial R&D. The pharmaceutical industry has demonstrated its willingness to take on the necessary risk and uncertainty that comes with developing medicines that address unmet needs. The unique challenges and dynamics of the antimicrobials market require unique measures to establish an economic environment that will incentivise ongoing antimicrobial R&D.

We therefore believe that the following principles combined with the strategies below will help to build a comprehensive response to the threat of AMR:

- An AMR strategy that involves a collaborative and coordinated response from a wide range of stakeholders across a variety of sectors, including the innovative medicines industry.
- A multi-faceted approach that addresses the issue, covering regulatory and reimbursement frameworks, incentives for R&D, diagnostics, vaccines, surveillance and stewardship. No single response will solve the issue, they all need to work in tandem.

Industry representation and collaboration

Addressing the rising threat of AMR requires a holistic and multi-sectoral ('One Health') approach, which includes regular and genuine collaboration between stakeholders. Industry has an essential role to play in both investing in the development of novel antimicrobial agents, and in working with the government and the medical community to bring them to market and ensure that they are used in the most appropriate way. Medicines Australia and its members continue to engage and partner with governments, academia, prescribers and patients at global, regional and national levels in this pursuit.

Key Asks

Medicines Australia and its members must have a seat at the table in developing AMR policy, in particular:

- With respect to the establishment of a specific subcommittee of the Australian Strategic and Technical Advisory Group on AMR (ASTAG). This subcommittee would consult and engage with relevant stakeholders on industry issues including R&D, commercialisation, reimbursement, registration, and associated push/pull incentives.
- Participation and further input into the formulation of the National AMR Strategy 2020 and beyond

Regulatory Framework

The Therapeutic Goods Administration (TGA) plays a critical role in ensuring the quality, safety and efficacy of medicines in Australia. Medicines Australia strongly supports the TGA in this endeavor. Ensuring access to new antimicrobials will require regulatory authorities to streamline and accelerate clinical trials required for regulatory review and approval of antimicrobials.

Key Asks

The following options could be considered to support the registration of novel antimicrobials:

- Update the TGA guidelines for priority review/provisional registration to allow for accelerated registration of novel antimicrobials for priority organisms of high public health importance and/or substantial impact of resistance.
- Waivers on registration fees
- Allow for different levels of data to support expanded indications (e.g. at other sites of infection) for approved antimicrobials, where appropriate, for example using:
 - PK/PD data
 - In vitro susceptibility data
 - Microbiological data
 - Real world evidence e.g. from case series, registries or adaptive clinical trial designs.

Reimbursement Framework

The lack of a viable market for antibiotic commercialization is turning industry away from R&D in the antimicrobial sector due to concerns over a lack of a viable market post product development. A recent article by news company Bloomberg illustrated the 'second valley of death in drug development' with the example of Achaogen Inc. Achaogen was a small firm that specialized in antibiotics, and it had benefited from push incentives for R&D. However, less than 12 months post launch of its new antibiotic to treat resistant organisms, they filed for bankruptcy, as they had sold less than \$1 million over that time period². This demonstrates that research funding needs to be coupled with a market for antibiotics when they get approved.

Whilst the current reimbursement system in Australia promotes the quality use of medicines, there is a need for more flexible procurement processes that preserve the principles of AMR. This is important as there are a number of challenges companies face when investing in the development of novel antimicrobials, such as:

- Antimicrobials are generally undervalued by reimbursement systems relative to the benefits they bring to society as lifesaving drugs, due to low cost price comparators which are often generic medicines
- Uptake of novel antimicrobials is slow, since they are usually used sparingly to preserve effectiveness
- There is no national reimbursement system for antimicrobials in Australia. Most antimicrobials that are required to treat infections are funded through the states via hospitals. Hospital budget constraints mean that cheaper antimicrobials are often used first, even when a novel antimicrobial might be more clinically appropriate

Due to these challenging market conditions, only a handful of antimicrobials have launched in Australia over the last decade, and there are novel antimicrobials that are available overseas which are not available in Australia, or which are severely delayed in launching e.g. tedizolid has been available in the US since 2014 but is not currently available in Australia. In addition, several large pharmaceutical companies have withdrawn from antimicrobial research, and there are only two Medicines Australia member companies that currently maintain antimicrobials portfolios. Targeted measures are required to create the market conditions that will enable a predictable and sustainable return on investment in novel antimicrobials to combat AMR.

Key Asks

Government should consider working with industry to develop novel business models to create more sustainable in-market dynamics, for example:

- Insurance licenses: annual licenses paid to a manufacturer to have access to a specific antibiotic, up to a specific volume. In this regard, institutions are fully in charge of stewardship of these medicines. This approach delinks the return on investment on an important medicine from the volume of the drug that's used, thus also achieving an important public health purpose as these are drugs that require stewardship to slow the rate of resistance.
- Market entry rewards: a series of predefined lump sum payments awarded to the developer after regulatory approval, delinking volume and revenue.
- A Federal funding mechanism for novel antimicrobials that treat priority organisms, e.g. a guaranteed government purchase of a defined supply of the antibiotic for national stockpile
- Removing the cost-effectiveness comparators for novel antimicrobials that treat priority organisms.
- Consideration of whether business models and funding mechanisms of the sort mentioned above would require some form of legislative solution. If the antimicrobials in question were to be used in the community, such mechanisms would not fit with the current legislative governance of the Pharmaceutical Benefits Scheme. As above, such novel business models and funding mechanisms do not preclude the application of health technology assessment, but there is the double difficulty of low cost generic comparators and availability via 'reserve stockpiles' or annual licenses which are outside of the usual 'paying for health outcomes' approach of health technology assessment (HTA).

R&D Incentives

To ensure that research and development resources are used effectively, a national AMR research agenda needs to be developed. The research agenda should identify research and development priorities and enable institutes to work collaboratively to fill knowledge gaps.

Pharmaceutical innovation is time consuming, risky and expensive, and antibiotic discovery is particularly challenging. As the market for novel antimicrobials is not viable, a range of both 'push' and 'pull' incentives is required to strengthen investment in R&D. Push incentives generally focus on removing barriers to the developer by decreasing the cost of investment in R&D (e.g. research grants). Pull incentives involve commitment of financial reward after a technology has been developed (e.g. through market entry rewards or intellectual property [IP] mechanisms).

Government currently does a good job on push incentives for research, for example AMR is one of the Medical Research Future Fund Priorities for 2018-2020, with the provision of research grant opportunities. However, significant challenges remain to ensure that compounds identified in basic research successfully translate, more emphasis is needed on product development where industry can be an important collaborator.

There are many international initiatives focused on the development of novel antimicrobials, examples include CARB-X, GARD-P and the Innovative Medicines Initiative's DRIVE-AB. Australia could explore how to contribute to these initiatives or learn from the models employed and consider local initiatives that are complimentary and not duplicative, whilst focusing on particular pathogens uniquely relevant to Australia.

Key Asks

- The Government to develop a national AMR research agenda
- Priority reviews for companies that bring novel antimicrobials to market, which are transferrable to their other brands
- IP mechanisms, such as transferable exclusivity extensions
- Explore feasibility of collaborating with international initiatives and public private partnerships focused on development of novel antimicrobials

Vaccines

In addition to the judicious use of antimicrobials and greater infection control measures, AMR stewardship must include more preventative measures such as vaccination. Vaccination can play multiple roles in AMR reduction strategies including:

- Reducing the use of antibiotics by preventing bacterial infections, e.g. conjugate pneumococcal vaccines
- Reducing the misuse of antibiotics by preventing viral diseases for which antibiotics are inappropriately prescribed, e.g. influenza vaccines
- Preventing antimicrobial resistant infections from being transmitted, e.g. pertussis and Hib vaccines
- New vaccines can also play a role in the prevention of multi drug resistant infections, e.g. *S. aureus*, *C. difficile* and *E. coli*.

To accelerate novel vaccine R&D, there is a need to engage all relevant stakeholders to clearly define the priorities for the development of new vaccines against AMR pathogens and to establish mechanisms to support this development. This may involve establishing robust and real time disease and AMR surveillance databases, ensuring that vaccine researchers select the right pathogens, and also enhancing funding for early research in epidemiology and immunology of AMR pathogens.

Diagnostics

Diagnostics are crucial for ensuring that patients with resistant organisms have rapid access to appropriate antimicrobials and reducing the unnecessary use of broad-spectrum antimicrobials. Medicines Australia urges Government to commit appropriate resources to support uptake of new and innovative diagnostic methods. Further, as new antimicrobials are approved, adequate support should be in place to allow laboratories to perform additional manual tests on appropriate samples during the delay to uptake in automated or innovative new testing systems.

In this way, unnecessary delays in adequate treatment may be minimized thereby avoiding poor outcomes associated with suboptimal therapies.

Key Asks

Medicines Australia urges the government to provide support for:

- Via the development of the national research agenda, the development of a priority list of diagnostics
- Microbiology laboratories, to allow for the uptake of new methods for rapid diagnosis
- The timely inclusion of new antibiotics in diagnostics practices

Surveillance

Understanding evolving bacterial resistance patterns is critical to addressing AMR. Surveillance programs help health systems to better plan and adapt their usage of antimicrobials and help the pharmaceutical industry to identify where new therapies are needed.

Australia has several excellent national surveillance programs, such as the Australian Group on Antimicrobial Resistance (AGAR) and the Gram Negative Sepsis Outcome Program (GNSOP). However, these programs require local resource support to allow for voluntary participation. Medicines Australia supports enhanced community and animal surveillance but encourages adequate resource support for existing surveillance programs and participation in clinical research.

Key Asks

To improve surveillance, Medicines Australia seeks:

- Resource support for national surveillance programs which allow for voluntary participation
- Data on hospital infections and the burden of resistance on hospital networks
- Delineation of data by ward and site of infection
- Data linkage between microbiology, antimicrobial history, patient clinical factors and outcomes
- Transparency of individual hospital data

Stewardship

Antimicrobial stewardship refers to coordinated actions designed to promote and increase the appropriate and judicious use of antimicrobials, as well as improve infection prevention and control, both of which are essential to slowing the emergence of resistance. Economic stewardship, where the more expensive products are used as a last resort, should not be the primary approach: Antimicrobial stewardship should be about using the right antibiotic for the right patient at the right time.

Key Asks

In order to improve antimicrobial stewardship, the government should:

- Ensure that stewardship is based on clinical need rather than cost

Medicines Australia is happy to discuss or provide further comment on any aspect of our response and we would appreciate ongoing engagement and collaboration on further developments. Medicines Australia is also able to facilitate and participate in a meeting with key stakeholders to explore the opportunity for private-public partnerships and market entry models for reward with respect to antimicrobial stewardship and research and development.

Please contact Betsy Anderson-Smith if you would like further clarification on any aspect of our submission (banderson-smith@medaus.com.au).

Yours Sincerely,



Dr Vicki Gardiner
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Medicines Australia

References

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