MSD 2020-2021 Budget Submission

Merck Sharp & Dohme (Australia) Pty Ltd, December 2019

SUMMARY

MSD is passionate about improving the health of Australians and has a long history of working with the Government to ensure that Australians have access to the latest innovations in medicines and vaccines.

The World Health Organisation has described antimicrobial resistance (AMR) as one of the key global health issues facing our generation. If no action is taken, it has been estimated[1] that 10 million lives a year could be lost as a result of AMR by 2050, exceeding the number of deaths caused by cancer (8.2 million). In Australia, a recent study[2] has found that on any given day, one in every ten acute adult inpatients has at least one hospital acquired infection.

Australia's first National Antimicrobial Resistance Strategy 2015-2019 is currently being reviewed and updated for 2020 and beyond. One of the key objectives of the current strategy is to promote investment in the discovery and development of new products to prevent, detect and contain AMR[3]. In support of the National Strategy, MSD is proposing the establishment of a new pilot fund for novel antimicrobials.

RECOMMENDATION FOR A PILOT FUND FOR NOVEL ANTIMICROBIALS

Investing $20M per year for three years in an innovative pilot for funding novel antimicrobials would demonstrate Australia's policy leadership in the face of a looming global health crisis.

Features of the Pilot

- A three-year pilot, using the de-linked model currently being explored by the UK, whereby reimbursement is not linked to the volume of antimicrobials sold.
- Two novel antimicrobials selected to participate, targeting priority pathogens.
- A pragmatic approach to valuation of the participating drugs.

Estimated Cost of the Pilot

- The cost will depend on the specific drugs that are chosen to participate in the pilot.
- A pragmatic valuation approach shows that the cost of funding one drug could be estimated at $10.4M per year.
- The total cost of the pilot would then be in the order of $20M per year, for three years.

Benefits of the Pilot

- Short term: two novel antimicrobials, targeting priority pathogens, would be available for clinicians to prescribe to the right patient at the right time, with no budget constraints.
- Long term: the pilot would encourage investment in research and development, and would also set an example for other countries to establish similar programs.

[1] Jim O'Neill, 2014, *Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations*

[2] Philip L. Russo et.al 2019, *The prevalence of healthcare associated infections among adult inpatients at nineteen large Australian acute-care public hospitals: a point prevalence survey*, Antimicrobial Resistance and Infection Control

[3] Department of Health and Agriculture, *Responding to the Threat of Antimicrobial Resistance: Australia's First National Antimicrobial Resistance Strategy 2015-2019*

ANTIMICROBIAL RESISTANCE – A GROWING THREAT

What is AMR?

Antimicrobials are medicines used to treat and prevent infectious diseases caused by pathogens such as bacteria, viruses, fungi and parasites. Antibiotics, which are used to treat bacterial infections, are one of the most important types of antimicrobials. AMR occurs when a pathogen evolves to survive antimicrobial treatment[4]. While such evolution is inevitable, AMR is developing more quickly due to the inappropriate use of antimicrobials. Action is needed to slow down the development and spread of AMR so that the antimicrobials we have continue to work for as long as possible.

Why is AMR a problem?

As explained by the Australian Group on Antimicrobial Resistance (AGAR): "AMR is a risk to patient safety because it reduces the range of antimicrobials available to treat infections. It also increases morbidity and mortality associated with infections caused by multidrug-resistant organisms. AMR 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." [5]

AMR is responsible for an estimated 25,000 deaths per year in the EU, and the loss to EU health care and productivity as a result of AMR is estimated at €1.5 billion annually[6]. The impact of AMR in Australia has not been quantified in these terms, however adjusting for population and currency this would equate to roughly 1,250 deaths and a $120 million loss to healthcare and productivity annually in Australia.

AMR can be slowed down through the judicious use of antimicrobials, a practice known as Antimicrobial Stewardship (AMS), but it cannot be stopped. New antibiotics are urgently needed to address growing resistance, however there are relatively few in development. Over the past two decades, there has been a significant decline in the number of companies conducting antimicrobial research and development. Today, only a handful of pharmaceutical companies have antibiotics in clinical development[7].

Challenges to developing new antimicrobials

Simply put, the market for novel antimicrobials is broken. In Australia there are 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 has emerged to older treatments. This immediately limits the usage of a new product and the recouping of any research and development costs.
- There is no comprehensive data of the national reimbursement system for antimicrobials in Australia. Most of them is purchased by individual hospitals, which have highly constrained budgets [8].

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[4] Jim O'Neill, 2014, *Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations*

[5] Australian Group on Antimicrobial Resistance; *Sepsis Outcome Programs, 2018 Report*

[6] European Medicines Agency, European Centre for Disease Prevention and Control, 2009, *Joint technical report: The bacterial challenge: time to react*, accessed 16 December 2019 <https://www.ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf> accessed 17 December 2019

[7] Bhatti, T et,al 2018, *A Perspective on Incentives for Novel Inpatient Antibiotics: No One-Size-Fits-All*, Journal of Law, Medicines and Ethics, p59

[8] Department of Health and Agriculture, *Responding to the Threat of Antimicrobial Resistance: Australia's First National Antimicrobial Resistance Strategy 2015-2019*

- The need for hospitals to manage their budgets means that the use of novel antimicrobials can be discouraged[9], even when they may be a more appropriate treatment for a patient than a generic antimicrobial.
- Novel antimicrobials are generally undervalued by reimbursement systems relative to the benefits they bring to society as indispensable, life-saving drugs, because of the low cost comparator, which is often generic[10].

MSD is one of the few remaining large pharmaceutical companies investing in antimicrobial research and development and wants to work with Government to help re-stimulate the market for these crucial therapies.

AN AUSTRALIAN PILOT WOULD SHOW GLOBAL LEADERSHIP

The UK's new approach to encouraging R&D investment

In order to stimulate the 'broken market' a new approach to funding is required. The UK recently launched a pilot 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[11]. This results in more predictable revenue for the manufacturer, and coverage for the health system in the event of disease outbreaks. In other words, companies are paid for antimicrobials based on their expected value to the health system, as opposed to the actual volume used.

Principles of the proposed pilot

In order to constrain the innovative fund concept to a workable pilot, the following principles are proposed:

1. The pilot should be reserved for 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 the World Health Organisation[12], and is a major emerging AMR threat in Australia[13]. 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.
2. The pilot should support the AMS principle of using the right drug for the right patient, for the right organisms, at the right dose, at the right time, so that usage is always based on clinical need and appropriate use rather than the cost of an antibiotic.
3. The pilot should recognise the broader social value of making novel antibiotics available, while at the same time preserving their use according to AMS principles.
4. The pilot should act as a signal to industry that the government is willing to create a stable market for novel antimicrobials.
5. The pilot should be truly national, with engagement and support from Federal, State and Territory Governments.

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[9] 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

[10] Neri, M., Hampson, G., Henshall, C., and Towse, A., 2019. *HTA and payment mechanisms for new drugs to tackle AMR.* OHE Research Paper, London: Office of Health Economics, accessed 17 December 2019 <https://www.ohe.org/publications/hta-and-payment-mechanisms-new-drugs-tackle-amr#overlay-context=publications/hta-and-payment-mechanisms-new-drugs-tackle-amr>, p. v,

[11] https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/antimicrobial%20guidance/AMR-launch-statement.docx p2 accessed 17 December 2019

[12] https://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/, accessed 17 December 2019

[13] 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

6. 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.

How the pilot would work

MSD is proposing a three-year pilot which would fund two novel antimicrobials, structured as shown in Figure 1.

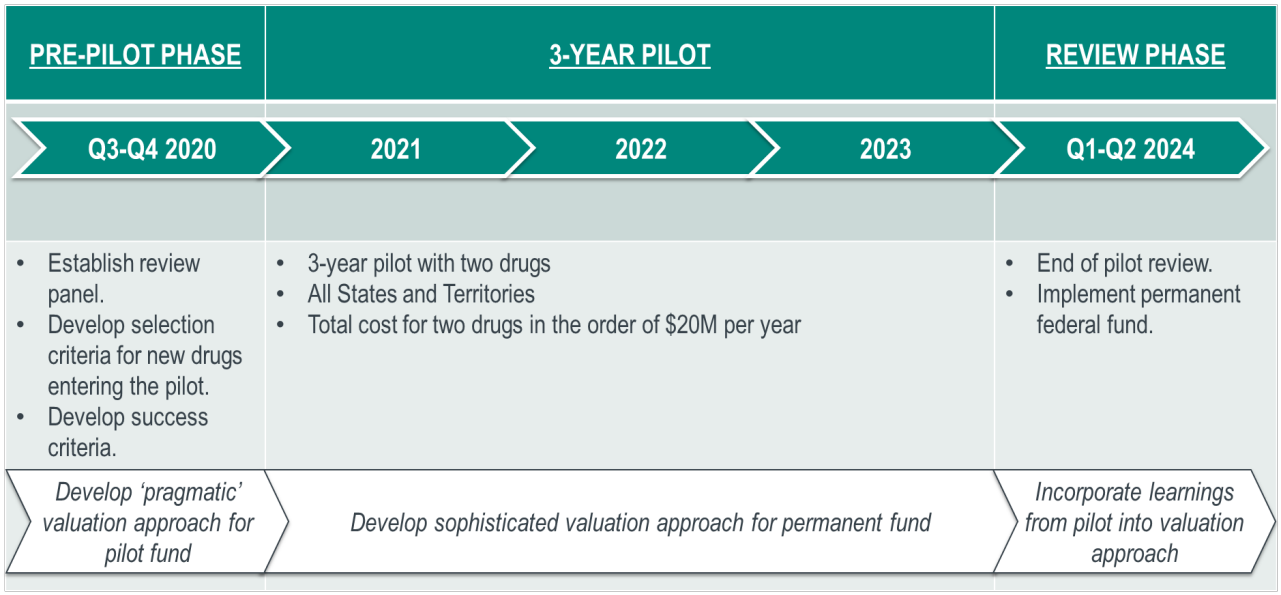

Figure 1 – Pilot Structure

- A pre-pilot phase would establish:
  - a review panel
  - selection criteria for drugs entering the pilot
  - a 'pragmatic' valuation approach for the drugs entering the pilot
  - success criteria for the pilot
  - surveillance and measurement requirements
- Sponsors would apply to enter the pilot, and the review panel would select two drugs (on the basis that the UK pilot is also being run with two drugs[14]) according to the agreed selection criteria, for example:
  - the drug targets a priority pathogen
  - susceptibility rates, resistance trends and RWE for the drug are available
  - the drug has the ability to overcome mechanisms of resistance
  - the drug is a new class or an extension of existing class
  - the sponsoring company has the ability to engage with the process over time
  - the sponsoring company can meet social responsibility and stewardship commitments
- For the chosen drugs, a set fee would be paid annually to the sponsor. The fee would be determined based on a pragmatic approach to valuing the drug (see the next section – note that the fee may be different for each drug chosen). The company would ensure that sufficient drug is made available to manage all anticipated infections within the established framework.
- The pilot would run for three years. During this time a more sophisticated valuation approach for the permanent fund would be developed.

[14] https://www.nice.org.uk/Media/Default/About/what-we-do/NICE- guidance/antimicrobial%20guidance/AMR-launch-statement.docx p2, accessed 17 December 2019

- A post-pilot review would be held, to inform the establishment of a permanent fund.

The short term benefit of this pilot is that two novel antibiotics would be available for clinicians to prescribe to the right patient at the right time, with no budget constraints.

The long term benefit of this pilot is that it would send a strong signal to the market that there is a reliable return for investing in research and development, and would also set an example for other countries to do the same.

A PRAGMATIC VALUATION APPROACH

The UK has already spent several years developing a workable model to determine the expected value[15] which takes into account their full value to society, including transmission value, insurance value, diversity value, enablement value, novel action value and spectrum value. This work is ongoing, as they are trying to establish a balance between the difficulty of the task, the complexity of the modelling required, and the use of expert opinion.

The purpose of this Australian pilot is not to develop an HTA approach to valuing novel antimicrobials, but rather to provide an opportunity for Government, clinicians and industry to work together on practical solutions for a pressing health issue. A simple, pragmatic approach can be taken to determining a value for the pilot, which would enable a pilot to commence whilst a more sophisticated valuation approach could be developed over the three years of the pilot.

Rather than try to calculate the broader social value of a novel antimicrobial, the pilot could look at a priority organism for which both an existing and a novel antimicrobial are available. The value of the novel antimicrobial would be the same as the existing antimicrobial, *except the value would be annualised over the life cycle of the drug*. This annualised approach addresses the issue that 'most of the use of the drug is likely to occur after patent expiry, when the build-up of resistance to existing drugs means that the new drug is now routinely used as a first line treatment … but it will be of no benefit to the innovator as the product will be off-patent and priced as a generic.'[16] In other words, uptake of novel antibiotics is slow, and rightly so, due to antimicrobial stewardship principles, so in order to provide a predictable return for manufacturers, some of the value needs to be pushed to the beginning of the life cycle. In addition, and in order to account for the broader social value of having novel antimicrobials available, a 10% 'social value' premium is also applied.

Using this approach, MSD has estimated that funding one drug in the pilot could cost in the order of $10.4M per year. The total could of the pilot would then be in the order of $20M per year.

[15] 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.* EEPRU, Policy Research Unit in Economic Evaluation of Health &Care Interventions, accessed 17 December 2019 <http://www.eepru.org.uk/wp-content/uploads/2017/11/eepru-report-amr-oct-2018-059.pdf>

[16] Neri, M., Hampson, G., Henshall, C., and Towse, A., 2019. *HTA and payment mechanisms for new drugs to tackle AMR.* OHE Research Paper, London: Office of Health Economics, accessed 17 December 2019 <https://www.ohe.org/publications/hta-and-payment-mechanisms-new-drugs-tackle-amr#overlay-context=publications/hta-and-payment-mechanisms-new-drugs-tackle-amr>, p. v

ABOUT MSD

For more than 125 years, MSD has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. MSD is a trade name of Merck & Co., Inc., with headquarters in Kenilworth, N.J., U.S.A. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, MSD continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world.

For more information visit www.msd-australia.com.au

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