MEDICINES Australia

Better Health through Research and Innovation

Submission to the Senate Select Committee into Funding for Research into Cancers with Low Survival Rates

March 2017

Senate Select Committee into
Funding for Research into Cancers with Low Survival rates
C/O Committee Secretary
Department of the Senate
PO Box 6100
Parliament House
Canberra ACT 2600

31 March, 2017

Via email: cancer.research.sen@aph.gov.au

Dear Sir/Madam

Re: Funding for Research into Cancers with Low Survival rates

Medicines Australia welcomes the opportunity to provide a submission to this important Senate Select Committee Inquiry.

The members of Medicines Australia invent, manufacture and supply innovative medicines and vaccines to the Australian community. Their medicines, discovered through global, as well as local research and development, contribute to the prevention of disease in Australia and help keep Australians healthy and productive. Our members are at the forefront of innovation and science in Australia. They directly employ around 15,400 Australians with many thousands more employed by it indirectly. Some 86 per cent of the Australian Government-subsidised Pharmaceutical Benefits Scheme (PBS) medicines made available in Australia, measured by value, are produced by our member companies.

The PBS is a critical feature in Australia's universal health scheme landscape. It is a scheme that is internationally recognised as world leading, because it helps to advance Australians' health care outcomes. All health care consumers in Australia, whether they have a rare disease or a more common one, should be able to have equitable access to treatments that help address their medical needs.

We recognise that resources are finite and that the Australian Government must deliver fiscally sustainable Budgets into the future, whilst also looking for opportunities to grow our economy.

We are very pleased that the Australian Government is encouraging science and innovation in Australia through, for example, Australia's first ever National Innovation and Science Agenda. We also welcomed the identification by Australia's Chief Scientist, entrusted with the oversight of a whole-of-government 10-15 year plan for growing and promoting innovation and science investment in Australia, of our sector as one of the five most promising growth sectors in Australia. We have recently signed a Memorandum of Understanding with MTPConnect, the growth centre for the medtech and devices sector.

Although our industry is a global one, we are proud that, despite significant international competition, our members conduct around 700 clinical trials in Australia, which are worth $450 million annually and which contribute around $AUD1 billion to the Australian economy each year. Innovative research partnerships between hospitals, research institutions and medicines companies support thousands of jobs for Australian scientists and researchers and we believe that with the right incentives, Australia can become an even stronger international innovation and investment destination. This is an essential backbone support that would help foster all kinds of medical research, including into treatments, cures, diagnostics devices and vaccines, without excluding rarer conditions and/or diseases for which there are few or no treatment options.

Our industry is responsible for the discovery, research and development of new and specialised medicines that are used to treat patients suffering from a range of different diseases and conditions - including low incidence (rare) cancers and brain cancer. As biotechnology and medical technology are global industries, Australia must compete to retain the R&D activity of local companies, as well as to attract international R&D activity into Australia. It is critical to maintain a stable, supportive and consistent policy environment in Australia in order to encourage life sciences businesses to make strategic decisions around R&D activity and bring additional investment into Australia.

We would highlight the role in Australia that government-led incentives can help play in ensuring small, medium and larger enterprises undertake, develop and extend their R&D activities in Australia. Research and development (R&D) activities, including pre-clinical testing and clinical trials, bring spill over benefits into the Australian health system by providing Australians with access to early stage therapeutics, diagnostics and medical devices during clinical trials and as final products; sometimes, this is the only and/or best option for people with rare and low survival rate cancers to access treatments, but this is not universal.

We consider that more can be done to foster growth of the life sciences sector in Australia, including early research into low survival cancers and rarer diseases.

> **Firstly**, that a number of specific initiatives can and should be deployed to increase clinical research in this area by generally improving Australia's international R&D competitiveness. This includes the establishment of an Australian Office of Clinical Trials to enable a national central point of contact to help drive harmonization and quality standards across the clinical trials sector.
>
> **Secondly**, that changes to the current access model, specific for medicines for rare and low survival conditions including cancer and brain cancer, are required to facilitate timely access to new and innovative medicines and technology; access is the key factor in improving health outcomes. This includes agreeing and accepting flexible evidentiary requirements which acknowledge the specific challenges of clinical trials in this area.

Our submission addresses the Committee's Terms of Reference (b) and (c) and is contained in Attachment 1 to this letter. Consistent with the concept that improving patient outcomes depends on both a) clinical trials and research to create acceptable levels of knowledge on new medicines new technologies, and, b) a system which can provide timely access to new medicines and technology by patients and their physicians, our submission is structured in two parts.
Medicines Australia welcomes the opportunity to work with the Committee and the Government in formulating appropriate clinical trial policies and access system enhancements.

Should you require any further information on this submission, I can be contacted at elizabeth.desomer@medicinesaustralia.com.au or on 02 6122 8525. Medicines Australia would of course be pleased to appear before the Committee should it decide to hold public hearings on the Bill.

Yours sincerely

Elizabeth de Somer
Director, Policy & Advocacy
(enc)

ATTACHMENT 1

Medicines Australia Submission to the Select Senate Committee Inquiry into the Funding for Research into Cancers with Low Survival rates

Executive Summary

The challenge of improving patient outcomes in low incidence (rare) and low survival cancers such as brain cancer requires both a) the creation of acceptable levels of knowledge on new technologies through clinical trials and research and, b) a system by which new technologies can be accessible to physicians and patients in timely way.

Medicines Australia therefore recommends that governments in Australia:

- Continue work to increase Australia's competitiveness and ability to attract more clinical trials on shore;
- Promote the conduct of research, including the development of biobanks, in rare and high clinical need diseases, such as cancers and brain cancers;
- Provide a policy environment that provides predictability to manufacturers and researchers, including the research-based pharmaceutical industry;
- Pursue systems to facilitate access to new technologies in rare and low survival conditions like cancer and brain cancer, both as a means of directly improving health outcomes and also to stimulate further investment in these disease areas;
- Continue to identify and implement ways to improve system efficiencies and changes to deliver faster access times for patients; and
- Commit to including specialist expert input, including oncologist and consumer input, as central to the decision making process for access to medicines.

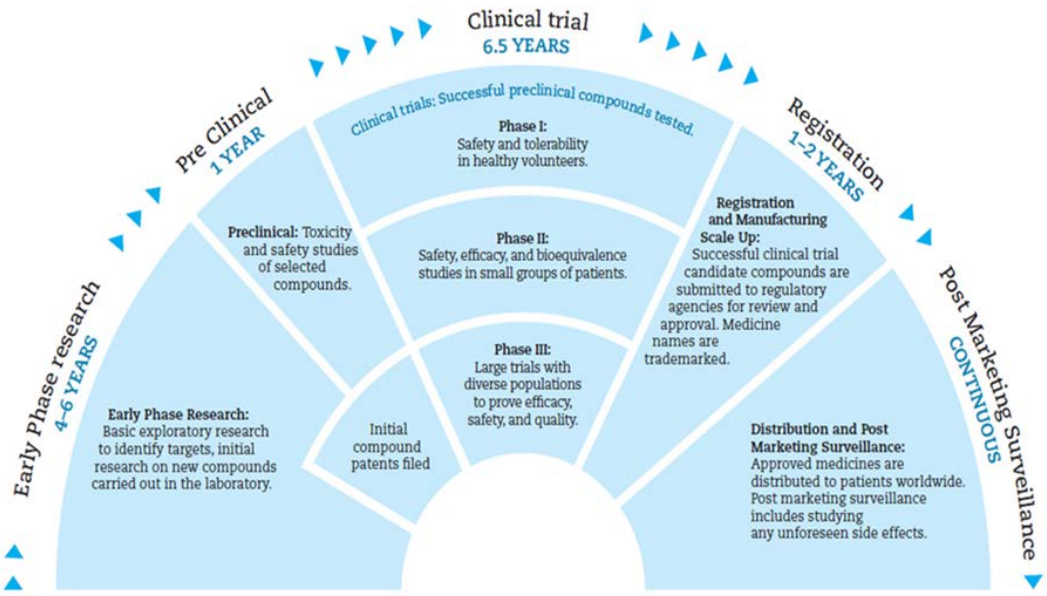
Introduction

The role of clinical research is pivotal in the process of bringing a medicine to patients, a reality reflected in Medicines Australia's pre-budget submission to the Australian Government[1] which describes the importance of clinical trials in Australia.

Clinical development is a long term project, as presented in

Figure 1, spanning a period of several years before evidence sufficient for registration is generated. For conditions with low survival rates such as cancer and brain cancer, this period can be longer and the prospect of generating sufficient evidence is more challenging compared to other conditions.

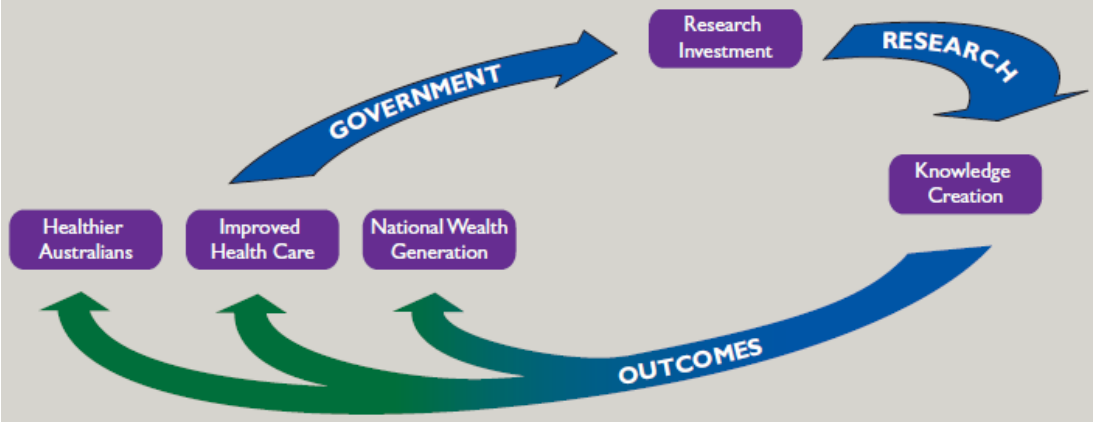
Figure 1: The process of clinical development from early phase, through to phase III, registration and post marketing



The National Health and Medical Research Council[2] (NHMRC) expresses the challenges facing low incidence (rare) and low survival cancers such as brain cancer in its opening statements on the importance of the translation of research into clinical practice: "*The creation of knowledge does not, of itself, lead to widespread implementation and positive impacts on health.*" This is illustrated in the NHMRC's Virtuous Cycle (
Figure *2*) which describes the relationship of research to health outcomes. This cycle is broken, or at least disrupted, when outcomes are not possible because of a lack of timely access.

[1] See Medicines Australia *Federal Budget Submission 2017/18* https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/02/Medicines-Australia-Budget-Submission-2017-18.pdf
[2] NHMRC website accessed 3 March 2017: www.nhmrc.gov.au/research/research-translation-0

Figure 2 - The NHMRC's Virtuous cycle illustrating the importance of the translation of research driven knowledge gains into health outcomes which, in turn, stimulates further research and knowledge gains.[3]



Specifically, the challenges facing rare and low survival cancers such as brain cancer lay at the heart of two specific aims implied by the virtuous cycle and reflected in this submission:

1) Increase and optimise clinical trial and other research activity to create acceptable levels of knowledge on new technologies; and

2) Ensure timely access to new technologies to enable a positive impact on human health.

These two aims must be considered as equally important in discussions of the drivers of survival improvements, and when contemplating what actions are required to accelerate survival improvements in cancers, or other diseases, where survival rates are poor.

It is unsurprising, then, that the Terms of Reference (ToR) of the Select Senate Inquiry perfectly parallel the two aims implicit in the NHMRC's challenge statement. Medicines Australia's submission is therefore structured in two parts to address each of the ToRs in the context of these two aims:

- Part 1 considers ToR (b): Medicines Australia makes recommendations relating to initiatives and policies which enable the creation of clinical research knowledge on new technologies, particularly in the context of low incidence cancers/diseases

- Part 2 considers TorR (c): Medicines Australia makes recommendations relating to the use of that knowledge to enable timely access to new technologies and thus achieve improved health outcomes

[3] *From: National Health and Medical Research Council Strategic plan 2007-2009 (https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/nh80.pdf : accessed 10 March 2017)*

Part 1: Term of Reference (b): Recommendations relating to initiatives and policies which enable the creation of clinical research knowledge on new technologies, particularly in the context of low incidence cancers/diseases

As the Australian peak body for the discovery-driven pharmaceutical industry, we have highlighted changes which are likely to facilitate increased clinical research funding/investment and activity from this sector, both in the context of low incidence cancers/diseases and for all clinical trial research more generally.

Part 1 of this submission, and ToR (b), correspond to the "Research Investment→Research→Knowledge Creation" segment of the virtuous cycle at

Figure *2* (above).

Medicines Australia recommends:

1.1 Continuing to work to increase Australia's competitiveness and ability to attract more clinical trials, overall, by:

- Understanding and acknowledging key factors which affect clinical trial competitiveness
- Implementing previous recommendations: Streamline trials approvals process and governance arrangements and implement other actions recommended by earlier reports on this issue
- maintaining the TGA's Clinical Trial notification system which is critical to maintaining competitiveness
- Establishing an Australian Office of Clinical Trials, being a national co-ordination unit, to enable a national central point of contact to help drive harmonization and quality standards across the clinical trials sector; this would entail working collaboratively with the Commonwealth, States and Territories

1.2 Increasing the conduct of research in rare and high clinical need diseases, including cancers and brain cancers by:

- Embedding clinical trials in clinical practice
- Increasing clinical trial participation through broadening awareness and coordinating patient access
- Developing new clinical trial approaches to increase participation
- Expand and coordinate biobanks and genomic registries to guide further research

1.3 Providing a policy environment that provides certainty and is supportive of research and the research-based pharmaceutical industry by implementing the recommendations of the Review of Medicines and Medical Devices Regulation and the Life Saving Drugs Program

1.1 Continue work to increase competitiveness of Australia and attract more clinical research

Understand factors which affect clinical trial competitiveness

Every year, around 700 new clinical trials are commenced in Australia by the medicines industry.

While Australia is well recognised for delivering high quality clinical trials, we are the fourth most expensive country in the world in which to conduct clinical trials.[4] This acts as a deterrent to undertaking clinical research in Australia. Some of the costs are attributable to inefficiencies that act as barriers to efficient initiation of clinical trials:

Lack of national harmonization of systems of clinical trial approval: The systems under which clinical trial sites in Australia are approved differ between states and territory. The approach to research governance can even differ between sites within states and territories. This is an avoidable inefficiency.

Inconsistent and slow start-up times: There is inconsistency in Australia in regard to trial start up times. In some cases it requires a relatively long time to set up and start a trial in Australia (30% of multi center trials require over 6 months to complete ethics approval[5]) and this is regularly identified as one of the most important reasons Australia is losing its competitive edge against other countries.

Implement previous recommendations made to the Australian Government

There is clear and universal good intent to improve clinical trials and Australia's clinical trial competitiveness. Some approaches have been identified but implementation has not progressed ideally, largely due to difficulties associated with coordination across states and other such barriers. One way of addressing this lack of alignment is the establishment of a national clinical trials office, discussed below. Nevertheless, implementation of previous recommendations, below, would also have a beneficial impact.

- In 2011, the Clinical Trials Action Group recommended a combined 30-day best practice benchmark for both ethics and research governance reviews.[6]

- The NHMRC has developed a 'Good Practice Process' for the site assessment and site authorization phases of clinical trials research governance. Following piloting of the Process at 16 sites throughout Australia, it was found that more than 100 days, on average, was able to be removed from the time taken for clinical trial commencement.

[4] Pharmaceuticals Industry Council, 2013, Benchmarking the Cost of Conducting Clinical Trials in Australia
[5] Medicines Australia (2014) *Proposed removal of red tape affecting the Australian Medicines Industry* Submission to the Parliamentary Secretary to the Prime Minister, Canberra.
[6] Commonwealth of Australia (2011) *Clinically Competitive: Boosting the Business of Clinical trials in Australia*.

Maintain the TGA's clinical trial notification system.

The Clinical Trial Notification (CTN and eCTN) system in Australia is an existing system which must be maintained as a basis upon which to build a competitive clinical trial environment. We understand that it is a very attractive feature for global investors.

Establish an Australian Office of Clinical Trials to help reduce inefficiencies

The national implementation of these identified improvements requires collaboration between different levels of government in Australia. This should continue and expand.

The clinical trials environment in Australia, however, is in need of further reform. Consequently, Australia would benefit from a national co-ordinating contact centre for clinical trials to implement national standards and roll them out nationally. Medicines Australia suggests that this could be achieved through establishing a National Office of Clinical Trials or similar dedicated entity. Medicines Australia is keen to contribute its knowledge and experience to establish such an office.

Medicines Australia does not underestimate either the size or the complexity of this objective and the difficulties faced in reaching agreement and harmonisation across the federation. The desire for streamlined ethics approvals, mutual recognition and centralised systems for governance have hit road blocks associated with the complexity of a federated system despite numerous studies and reports dating back a decade identifying these as 'barriers' to clinical trials/research.[7]

Medicines Australia was pleased to learn of the states' and territories' recent commitment to endorse a revitalised agenda to streamline the conduct of clinical trials in Australia (which was outlined in the COAG Health Council's recent communique). We are further pleased to see the Commonwealth's $7 million investment into this initiative.

1.2 Increase conduct of research in rare and low survival diseases such as cancer and brain cancer

Increasing the overall clinical trial competiveness of Australia itself can positively impact the conduct of research for rare and low survival conditions like cancer and brain cancer. However, some specific actions can effectively support this aim.

Embedding clinical trials in clinical practice

We consider there is a role for clinicians in rare disease areas to be made more aware of the clinical trials options that might be available to their patients who are suffering from rare diseases. A national strategy to ensure physicians are aware of available clinical trials, and to embed these as options to be considered for their patients, could both assist in trial recruitment and provide patients and physicians with access to new, though experimental, medicines and technologies.

[7] McKeon S. 2013. "Review of Health and Medical Research". Australian Government, Canberra

Increasing clinical trial participation: broaden awareness and coordinating patient access

Patient recruitment is critical to the success of every clinical trial, and this is more acutely difficult for rare or low survival conditions. Mechanisms to promote clinical trials awareness and opportunities to the public at large are important, but are limited. Further, coordination of clinical trial access pathways between hospitals or institutions (i.e. enabling a patient in one hospital to be referred to another because of an available clinical trial) can be ad hoc. For these reasons, difficulties in recruiting patients to clinical trials remain a barrier to their initiation.

Increasing awareness: Clinical Trial Networks led by highly experienced clinicians operate in Australia and can assist in many areas. The Australian and New Zealand Clinical Trials Registry (ANZCTR.org.au) website is also an important tool for communication of existing trials. However, these could be the subject of more active promotion and coordination. We understand the Australian Government will develop a national communications strategy to increase patient identification and eligibility, which is welcome, but is still awaited.

National e-heath records might also play a role in helping to promote awareness of clinical trials to the public, but progress in this area has been slow. Nevertheless, the opportunities which digital strategies and big data type approaches represent should be explored.

Coordination of clinical trials: There is a lack of organised trials networks beyond a single institution and this prevents, for example, inter-hospital referrals of patients into clinical trials in neighbouring institutions. Thus initiatives which coordinate the execution of clinical trials at a national level can be extremely impactful, as experienced in the United Kingdom where the establishment of a research network increased trial participation more than three-fold[8]. Once again, the proposed clinical trials office described above can greatly improve this situation.

New clinical trial approaches

Meanwhile, initiatives designed to overcome other barriers to patients' access to clinical trials are underway. One key initiative in which Medicines Australia is involved is the Teletrials project with MTPConnect,[9] in collaboration with the Clinical Oncology Society of Australia (COSA). The Teletrials project is specifically designed to help overcome geographic and location barriers in order to increase trial participation. This can be especially impactful for rare and low survival rate diseases like cancer and brain cancer.

[8] Stead, M. et al. Strengthening clinical cancer research in the United Kingdom. Br J Cancer. 2011 May 10; 104(10): 1529–1534

[9] MTPConnect is a not-for-profit body, established in Nov 2015 by the Australian Government, which aims to turn Australia's world-leading research into medical technologies, biotechnologies and pharmaceuticals. The ten-year Sector Competitiveness Plan released in December 2016, observes that it has proven difficult to attract private capital during pre-clinical and clinical stages of development in Australia. These have become known globally as the twin valleys of death. In these "valleys", the cost of further translational research or early-stage clinical trials is substantial, and the risks are still too high to draw in sufficient funding from private investors alone.

Another type of innovative trial design which is being explored to support access to treatments for rare diseases are the so-called "basket studies" which enrol a patient group with a mix of tumour types that have common biomarkers, rather than conducting studies in each tumour. These studies are not currently accepted as an evidence base by regulators and payers in Australia, unlike in the EU and USA. This means that Australia's ability to attract such studies, as they grow in prevalence internationally, will reduce relative to countries which accept such evidence.

Expansion of biobank and genomic registry

The Austrade Clinical Trials booklet[10] describes biobanks as a collection of biological specimens which can facilitate proof of concept research for discovery of biomarkers, or the validation of previously identified markers. At the same time, the federal government is consulting on the development of a national genomic policy[11]. Together, these two initiatives have the potential to provide a valuable pathway to evidence generation for rare and low survival conditions.

1.3 Providing a supportive policy and access environment to encourage research investment from the discovery-driven pharmaceutical industry

The broader policy environment is also challenging the investment decisions made by pharmaceutical companies. Increasing levels of uncertainty caused by a single payer system, as well as inconsistent approaches to intellectual property, aggressive pricing policies and an unpredictable policy environment, are among the issues which Medicines Australia finds to be of some concern. The recent amendments to the R&D Tax Incentives in the Omnibus Repair Act 2016 are a case in point (this Act was considered by Parliament in September 2016 – our submission to that inquiry can be found here).

To ensure ongoing R&D investment, MA strongly advocates for a policy environment that provides predictable signals to support research and the research-based pharmaceutical industry. Some examples are outlined below.

Implementation of the recommendations of Review of Medicines and Medical Devices Regulation and the Life Saving Drugs Program

Ensuring timely, equitable access to medicines on the basis of clinical research evidence is an important factor in achieving health outcomes. It also is important in attracting further investment in R&D and therefore plays a key role in the virtuous circle described above.

In this context, encouraging developments are emerging, such as the implementation of the Review of Medicines and Medical Devices Regulation (MMDR), which aims to tangibly improve the time to market authorisation - particularly for high-priority medicines, which may include treatments for rare and low survival diseases such as brain cancer.

[10] Clinical Trials: www.austrade.gov.au/ArticleDocuments/2814/Clinical-Trials-Capability-Report.pdf.aspx. Accessed 24 March 2017

[11] https://consultations.health.gov.au/genomics/national-health-genomics-policy-framework/

Medicines Australia welcomes the implementation of the Review's recommendations, but notes that this initiative focuses on accelerating the process for registration rather than defining the appropriate evidentiary requirements. Similar process improvements to expedite broad patient access via the Pharmaceutical Benefits Scheme (PBS) or some other access model (discussed further below). A look forward to positive outcomes of the Life Saving Drug Programme (LSDP) Review which we hope will further facilitate subsidised timely and equitable access to rare and very rare diseases.

Part 2: Terms of Reference (c): Recommendations relating to the pursuit of systems to facilitate access to new medicines, tests, devices and techniques and thus achieve improved health outcomes.

Part 2 of this submission and Term of reference (c) are directly relevant to the "Knowledge Creation → Outcomes" segment of the NHMRC's virtuous cycle (Figure *2*, above).

Crucially, the generation of knowledge through clinical research is not enough on its own to bring about improvements in health outcomes. In considering the Inquiry's ultimate aim of increasing survival in low survival cancers including brain cancer, it is simply not sufficient to enhance clinical trial systems without also improving translation of the knowledge into practice. This can be achieved through enhancements to the PBS access system.

This precise issue of timely PBS access to medicines was the subject of the 2015 Senate Inquiry 'into the availability of new, innovative and specialist cancer drugs'. The Committee's report, and MA's submission[12], presented a number of recommendations that are extreme relevant for the present inquiry and are reproduced below.

Importantly, adoption of some of the Report's recommendations (including Managed Access Programs and PBAC submission pathways) is progressing due to positive and constructive collaboration between key stakeholders, including Medicines Australia and the Department of Health.

[12] See Medicines Australia (2015) *Submission to the Senate Inquiry into the Availability of New, Innovative and Specialist Cancer Drugs in Australia* https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/02/20150227-sub-Medicines-Australia-submission-to-senate-inquiry-into-cancer-medicines-FINAL.pdf.

Medicines Australia recommends:

1. Pursue access to new technologies in rare and low survival conditions like cancer and brain cancer despite the complexity and difficulties of generating data, by working with industry and other stakeholders to:

- develop fit for purpose HTA processes which allow more flexible evidentiary requirements which take into account the clinical and ethical complexity which are often specific to trials of cancer medicines
- agree on a role for innovative trial designs and real world evidence, and how issues such as low patient numbers or treatment switch in clinical trials will be addressed - rather than denying PBS access on the basis of uncertainty in the evidence.
- develop additional access models for medicines for rare or low survival conditions like cancer and brain cancer

2. Continue to identify and implement ways to improve system efficiencies, as well as changes to deliver faster access times for patients by

- Implementation of the recommendations of MMDR
- Building on the MMDR and extending enhancements to the PBS system by streamlining co-dependent evaluation process (establish a single Committee) and allowing PBS submissions to be triaged to differing Pathways based on complexity and clinical need.

3. Commit to incorporate specialist expert input, including early oncology and consumer engagement, as central to the decision making process

2.1 Pursue timely access to new medicines and technologies for rare and low survival conditions like cancer and brain cancer

Provide for evidentiary and decision flexibility

The Australian system for determining which medicines should be reimbursed was implemented 20 years ago. There has been significant cooperative effort expended recently to update the PBAC guidelines, but more is needed to ensure Australian evaluation approaches are consistent with world's best practice. For example, overseas guidelines allow for adoption of a societal perspective, and the United Kingdom's National Institute for Health and Care Excellence (NICE) have recently developed technical papers on the use of real world data for reimbursement decision-making.[13]

Despite this effort to improve the system generally, it has not yet fully adapted to the changes in the development of medicines and diagnostic technologies for rare or low survival cancers such as brain cancer. Specifically, the evidentiary requirements for

[13] http://www.nicedsu.org.uk/Real-World-Data-RWD(3026863).htm

cancer do not take into account the clinical and ethical complexity which is often specific to trials of cancer medicines.

An excellent example of this is in relation to treatment-switch behaviour,[14] which is common in cancer trials for ethical reasons, yet which has a confounding effect on the demonstration of overall survival in such studies. There are internationally accepted techniques to adjust for this crossover but these methodologies have been considered inappropriate by PBAC in certain circumstances because of the associated uncertainty. Overall survival is clearly a key outcome and failure to agree on how to deal with this crossover effect of cancer trials is a barrier to timely access.

Additionally, the system is insensitive to the complexity of specialised cancer medicines which treat small patient populations, and has limited pragmatic solutions to address uncertainty. For example the presentation of a randomised controlled clinical trial which has sufficient patient numbers in at least two arms to reach a statistically significant outcome (and so minimise uncertainty) may not be possible in rare cancers, yet achieving timely access in the current system largely depends on such data.

These complexities are often inevitable characteristics of studies in rare and low survival cancers, whose trials are regularly affected by low patient numbers or treatment switch. Acceptance of this fact, and agreement on an alternative approach which incorporates flexible evidentiary requirements and decision criteria for these medicines would represent a critical and significant advancement. This would increase patient access and, subsequently, enable realisation of health outcomes.

Agree on the role of new trial designs

Innovative trial designs are being explored to support access to treatments for rare diseases, where it is not feasible to conduct randomised trials. Studies known as “basket studies” look at a patient group with a mix of tumour types that have common biomarkers, rather than conducting studies in each tumour. However, such studies are not currently accepted as an evidence base by the Therapeutic Goods Administration, the Pharmaceutical Benefits Advisory Committee (PBAC) nor the Medical Services Advisory Committee (MSAC), although they are more acceptable by EU and USA regulators. There needs to be further discussion on the role of these types of basket studies when making decisions on access to treatments for rare diseases, especially as there is some excellent research currently being conducted in Australia using these types of trial designs.

Real World Evidence

The flexible approach to reimbursement can be supplemented with the collection of real world evidence. Medicines Australia acknowledges that discussions are ongoing with the Department in this area and encourages continued discussion on a workable approach.

[14] Henshall, C., Sansom, L et al. “*Treatment switching occurs when patients in a randomized clinical trial switch from the treatment initially assigned to them to another treatment, typically from the control to experimental treatment*”. International Journal of Technology Assessment in Health Care, 32:3 (2016), 167–174.

A regulatory and reimbursement system that accepts more flexible evidentiary requirements, as well as a system that has the infrastructure to link existing clinical datasets and develop a centralised registry to capture real world health outcomes is a vastly more preferable approach than the denial of PBS access on the basis of evidentiary uncertainty.

Initiate dialogue on new access models

The proposition that a different or flexible level of evidence be applied to inform PBAC decision may not represent a solution in all instances.

Specifically, it is not uncommon for medicines to be acknowledged by PBAC as being effective in fulfilling a clinical need, but be rejected because of unacceptable cost effectiveness. In such instances, dialogue between government, patients and industry is needed to determine if there are other models or arrangements that can achieve access to these medicines.

2.2 Continue to identify and implement ways to improve system efficiencies/ changes to deliver faster access times for patients

Implementation of the recommendations of the MMDR

The recommendations arising from the MMDR, which will expedite access for some high priority medicines, are consistent with both Medicines Australia's recommendations and the recommendations of the previous Senate report itself. Medicines Australia is strongly encouraged by the developments from a regulatory perspective. This is, indeed, the first step in the process of translating research-derived knowledge into health outcomes. The next step is the acceptance of more fit-for-purpose evidentiary requirements for rare cancers, where it is challenging to conduct controlled clinical trials.

Build on the improvements being delivered by the MMDR and ensure advances extend to PBS

One effect of the MMDR is the reduction in time to registration for high-priority medicines, which may be medicines for rare and low survival cancers. However, this regulatory enhancement will put further pressure on the PBS reimbursement system. Specifically, some medicines will be registered more quickly and with a more limited dataset compared with the current situation. In such instances, it will be necessary to adjust the PBAC and MSAC system of decision making; failure to make any adjustment will result in an increase in the time between TGA approval and PBS availability and this is counterproductive to the achievements of the MMDR.

Streamline the PBAC/MSAC evaluation system: One specific example of extending the improvements of the MMDR to the PBS would be to streamline the evaluation and decision making process for co-dependent medicines (medicines for rare or low survival cancers often rely on the use of a diagnostic to identify the appropriate patient population). Australia has one of the lengthiest assessment processes in the world for

these technologies and MA's 2015 submission to the MBS Review Taskforce[15] identified the following reasons behind this:

- a separate recommendation is required from two Committees (MSAC for the test, and PBAC for the medicine), each with differing meeting schedules and underpinned by separate legislation;
- evidentiary expectations are high for both the test and medicine, meaning that submissions for co-dependent applications are complex, and invariably result in longer timeframes to listing when compared to medicines that do not require an associated test

The system could be streamlined by requiring application and approval through a single committee.

Achieve a PBAC submission Pathways system: Discussions on another approach to increase efficiency are progressing at present between the Department of Health and Medicines Australia. The aim of these discussions is to identify ways of assigning PBAC submissions to differing evaluation pathways based on complexity, clinical priority (including for rare and low survival diseases) and budget impact. This would allow more appropriate deployment of resources to focus on high need medicines and less resource for low complexity submissions. This approach is consistent with recommendations of the previous Senate report and has clear potential to provide a continuation of the efficiency gains from the MMDR.

2.3 Incorporate consumer and specialist expert input into the decision making process

Medicines for rare and low survival cancers are as variable as the type of cancers they are used to treat. This, and the speed with which treatment regimens are evolving, means that early inclusion and engagement with specialist oncology expertise, specific for the medicine being considered, would benefit the PBAC/MSAC decision making process.

Similarly, consideration of the patient-level impact of a medicine in a particular condition should be incorporated into PBAC/MSAC decision making. This can be achieved by securing a stronger consumer voice to provide input to the decision making process about the reimbursement of individual cancer medicines.

Further, from a broad perspective, a strong Consumer voice can provide input to the decisions about what the system of universal access should fund in alignment with community values.

[15] See Medicines Australia (2015) Submission to the MBS Review Taskforce https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/02/20151101-sub-MBS-review-2015-final.pdf

ATTACHMENT 2

Senate Select Committee: Terms of Reference

The impact of health research funding models on the availability of funding for research into cancers with low survival rates, with particular reference to:

a. the current National Health and Medical Research Council funding model, which favors funding for types of cancer that attract more non-government funding, and the need to ensure the funding model enables the provision of funding research into brain cancers and other low survival rate cancers;
b. the obstacles to running clinical trials for brain cancers and other cancers with relatively lower rates of incidence, with regard to:
    i. funding models that could better support much-needed clinical trials, and
    ii. funding support for campaigns designed to raise awareness of the need for further research, including clinical trials;
c. the low survival rate for brain cancers, lack of significant improvement in survival rates, and strategies that could be implemented to improve survival rates and;
d. other relevant matters.