Submission to:

Standing Committee on Health, Aged Care and Sport

Inquiry into approval processes for new drugs and novel medical technologies in Australia

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Executive Summary

Comments on each Term of Reference are summarised below in **Table 1**.

Table 1 - Short summary of the comments for each Term of Reference (ToR)

Main comments
ToR 4: whether the approval process for new drugs and novel medical technologies, could be made more efficient…through greater use of international approval processes, greater alignment of registration and reimbursement processes or post market assessment.
It is not unusual for submissions for health technologies for use in areas of high unmet need to be acknowledged by PBAC/MSAC as being therapeutically valuable compared to the alternatives, but where for various reasons, a recommendation cannot yet be made. In most cases, after subsequent submissions and negotiations, such health technology is eventually reimbursed. However, it is unsatisfactory from the patient's perspective that a technology which is acknowledged as providing additional value in an area of high need, can still take many months or more to become available. Building on the PBAC's Dec 2018 recommendation to the Minister, an approach is proposed which would provide interim access to health technologies for populations with high and unmet clinical need, while the PBAC/MSAC evaluation is ongoing. The approach proposes that interim funding be based on both the company's requested price and the PBAC/MSAC's view of the justified price at the time, and that interim access be available until the PBAC/MSAC process is successfully completed, or until a specific time has elapsed. Importantly, conditions of the proposed interim access commit the parties to ensuring that, if a resolution is not achieved, no patient who received treatment in the interim access period will be required to cease therapy. Though there are many more details to be identified and addressed, it is hoped that the specifics and options provided can stimulate discussion and changes which will help Australians dealing with conditions which are rare or where there are few existing options.
Additional comments
ToR 1: The range of new drugs and emerging novel medical technologies in development in Australia and globally, including areas of innovation where there is an interface between drugs and novel therapies
It is reasonable to expect an influx of new technologies, including gene therapies and co-dependent technology, over the next several years. Many of these will likely represent important advances for patients across a range of areas, including rare and high need conditions. Given the differing regulatory and pricing systems globally, and the potential of expanding international reference pricing (by the USA), Australia should expect that at least some of these technologies will challenge the current levels of cost-effectiveness. A system should be put in place to proactively identify high need medicines and to work with the relevant company to ensure these are brought to Australia
ToR 2: Incentives to research, develop and commercialise new drugs and novel medical technologies for conditions where there is an unmet need, in particular orphan, personalised drugs and off-patent that could be repurposed and used to treat new conditions
Re-purposing of off-patent medicines is possible and would require coordination and, in some cases, incentives for companies to undertake the required steps. One approach may be to identify medicines which can be re-purposed, and to engage with the relevant companies in a collaborative way to provide access to patients (which could require a registration submission, and a reimbursement submission). In regard to the general concept of offering incentives, the aim should be to achieve more rapid patient access to high need health technology. As discussed in ToR#4, patient access to important new technology in areas of high and unmet need could be hastened by providing interim access while the PBAC/MSAC evaluation is ongoing.
ToR 3: Measures that could make Australia a more attractive location for clinical trials for new drugs and novel medical technologies
Any additional measures which aim to attract further clinical trial activity to Australia should consider firstly, the current level of government support - which is substantial - and, secondly that clinical trials are themselves not acceptable substitutes for PBS/MBS listing which is the most appropriate way to achieve broad and equitable patient access.

The Author of this submission

This submission is provided by Michael Smith. I am a consultant in the medicines reimbursement system in Australia, the founding member of the Reimbursement Expert Advisory Panel (REAP) and was previously employed in the pharmaceutical industry for 25 years, up until the end of 2018.

The opinions and suggestions here are my own and are not intended to represent either the REAP, or any company or government entity.

The aim of the comments herein is to assist the Committee as much as possible to ensure Australia continues to access new medicines and novel medical technologies in a timely manner.

Introduction

This submission is largely focussed on Term of Reference (ToR) #4, which builds upon a previous Pharmaceutical Benefits Advisory Committee (PBAC) recommendation to the Minister[1] to seek further information on options for providing subsidised access to medicines considered by the PBAC to meet a high and unmet need, while an application is under consideration. However, additional comments to ToR #1-3 are provided in Attachment 1.

Progress has been made

It is important to acknowledge that the efforts of many people in government, in the Department of Health, in health technology companies, physicians and individuals, including patients and their families, have played a role in the progress that has happened or is happening in the system in Australia. Senate inquiries and reports have examined the processes which are undertaken to make new health technologies available to Australians[2, 3, 4] and there were 205 submissions to the 2015 Senate Review on availability of new cancer drugs[3], illustrating the importance of this matter to many people and groups across Australia.

Improvements to the timings of and procedures for evaluating medicines by the Therapeutic Good Administration (TGA) were stimulated by the 2015 Review of regulations[4] and were welcomed by patients, their families and their physicians.

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[1] PBAC Advice to the Minister on PD-(L)1 Inhibitors, December 2018 (point 4.4): https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/agenda/pdf/august-2018-special-meeting/pbac-pdl1-report-to-minister.pdf

[2] Select Committee into funding for research into cancers with low survival rates (2017): https://gicancer.org.au/wp-content/uploads/2017/12/Low-Survival-Cancers-Funding-Parliamentary-Senate-Inquiry-Report.pdf

[3] Community Affairs References Committee, inquiry into the availability of new, innovative and specialist cancer drugs in Australia (2015): https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Cancer_Drugs/Report

[4] Review of Medicines and Medical Devices Regulation (2015): https://www1.health.gov.au/internet/main/publishing.nsf/Content/Expert-Review-of-Medicines-and-Medical-Devices-Regulation#report1

The PBS Process Improvements[7] aim to, among other things, support timely access to new medicines – especially for medicines which represent added therapeutic value for rare diseases and conditions where there is high and unmet clinical need. If these improvements are implemented successfully, they will expedite PBAC recommendations and PBS listings of these types of medicines when residual issues are resolvable.

Challenges still exist

Nevertheless, challenges remain in making medicines available to Australians in a timely manner, including for rare conditions or where there is a high and unmet clinical need.

One recent example of a challenge which will likely be raised with the Committee is the possibility of price referencing between the United States of America and Australia[5]. One view is that this represents a challenge to access in Australia because, if medicines' prices in Australia are referenced by the USA (i.e. prices in Australia are used as reference points to adjust prices in the USA), it will delay or prevent availability in Australia. This is because Australia is a small market globally, and in comparison to the USA.

While this potential development is beyond the Scope of this Inquiry, it will be seen by some submitters as impactful. Because reference pricing by the USA would be a new development, its impact remains to be seen.

Regardless, previous Senate Inquiries[3] have received submissions[6] describing delays to access. The developments and initiatives which have arisen from these Inquiries aim to reduce delays – especially for medicines with added therapeutic value.

The idea of providing access to some health technology while an evaluation is ongoing, initially mentioned by the PBAC, may be a way to provide more rapid access in conditions of high and unmet medical need. This is discussed further and built upon in ToR#4, below.

Addressing the Terms of Reference

This contribution will focus on Term of Reference #4, and comments to Terms of Reference 1, 2 and 3 are provided in **Attachment 1**.

ToR#4 - whether the approval process for new drugs and novel medical technologies, could be made more efficient…through greater use of international approval processes, greater alignment of registration and reimbursement processes or post market assessment.

This submission, which builds upon an idea previously raised by the PBAC, proposes an approach to hasten patient access to new drugs and novel medical technologies (herein referred to as health technologies) that:

- have been previously considered by PBAC/MSAC but not recommended for reimbursement;

[5] Executive Order on Lowering Drug Prices by Putting America First (13 September 2020): https://www.whitehouse.gov/presidential-actions/executive-order-lowering-drug-prices-putting-america-first-2/

[6] For example, Submission 108 – Medical Oncology Group of Australia

- PBAC/MSAC consider are applicable to a population/condition which has a high clinical need, and that the clinical need is currently unmet; and
- PBAC/MSAC consider are likely to address that unmet clinical need.

This submission is not about health technologies that:

- have not yet been considered by PBAC/MSAC; and
- are for a population which PBAC/MSAC consider is not at high or unmet medical need.

Further, this submission does not propose any changes to the processes and approaches that are already in place to evaluate health technologies for reimbursement (i.e. the PBAC or MSAC submission processes), including the ongoing PBS Performance Improvements changes[7], managed access programs and others. As described further in this submission, the existing processes would continue as normal, in parallel with the interim access approach.

Background

In December 2018, the Pharmaceutical Benefits Advisory Committee (PBAC) recommended to the Minister that advice should be sought on options for providing subsidised access, while an application is under consideration, to medicines considered by the PBAC to meet a high and unmet need[1]. In March 2019, the Minister responded[8] and instructed the department to "*undertake preliminary investigations of legislated options for, and provide advice to Government within six months on…subsidised access to Therapeutic Goods Administration (TGA) registered medicines that offer a therapeutic advance for conditions where there is a high and unmet clinical need, while the PBAC is considering an application*".

Though the specifics of the PBAC's thought process were not revealed, this is potentially a highly valuable suggestion that could hasten access to new high value medicines by around 12 months[9].

It is not unusual for submissions for medicines for use in areas of high unmet need to be acknowledged by PBAC as being therapeutically valuable compared to the alternatives, but where for various reasons, a recommendation cannot yet be made. In such a situation, further data may be needed to demonstrate superiority, other changes to the submission are needed, or a price reduction is required (and sometimes all of these) for listing to proceed. In most cases, after one or more resubmissions followed by pricing and listing negotiations, agreement is eventually reached and listing proceeds.

However, while reimbursement is eventually achieved, it is likely to be very disappointing from the patient's perspective that a health technology which is initially acknowledged as providing additional value in an area of high need, can take many more months to years to be listed. This is also likely to be unsatisfactory to the PBAC/MSAC, the technology company, and most other stakeholders. Consequently, the idea of providing subsidised access to some health technologies while the PBAC/MSAC evaluation process is ongoing has merit.

[7] https://www.pbs.gov.au/general/process-improvements/Fact-Sheet-PBS-Process-Improvements-Stage-2.pdf
[8] https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/agenda/pdf/august-2018-special-meeting/Minister-Hunt-response-to-Professor-Wilson-PD-L-1-report.pdf
[9] Estimate – based on an assumption of two resubmissions for an originally rejected submission

Subsidised access would likely be applicable only to a limited number of health technologies that have been considered but not recommended for reimbursement. Specifically, those that are for a population/condition which has a high and unmet clinical need, and where the PBAC/MSAC considers that the drug/technology is likely to address the unmet clinical need.

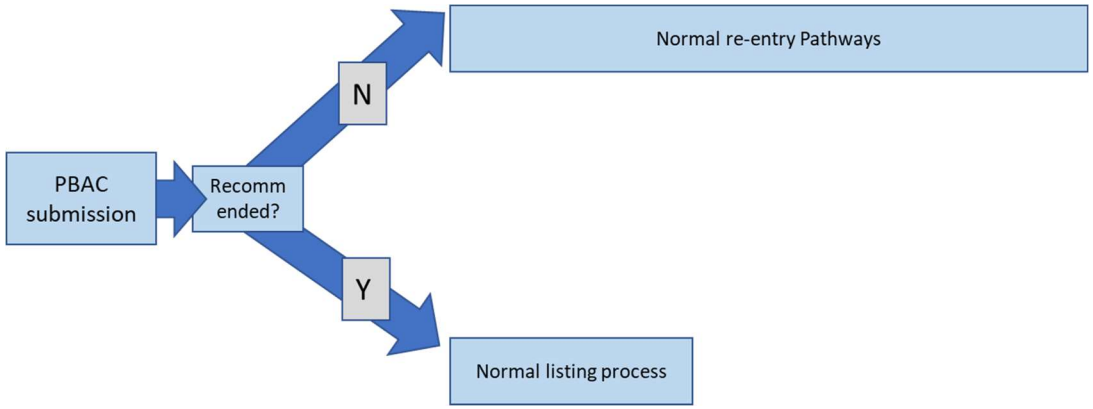
To reiterate, this idea is not about new health technologies that have not yet been considered by PBAC/MSAC, or that have been considered by PBAC/MSAC to be for a population which is not sufficiently high or currently unmet medical need. Further, this idea is not intended to replace or affect the current processes and approaches that are already in place to evaluate health technologies for reimbursement, including the emerging PBS Performance Improvements changes, managed access programs and so on. Indeed, these would continue, unaffected by, and parallel to the proposal detailed below.

Interim access to high value medicines

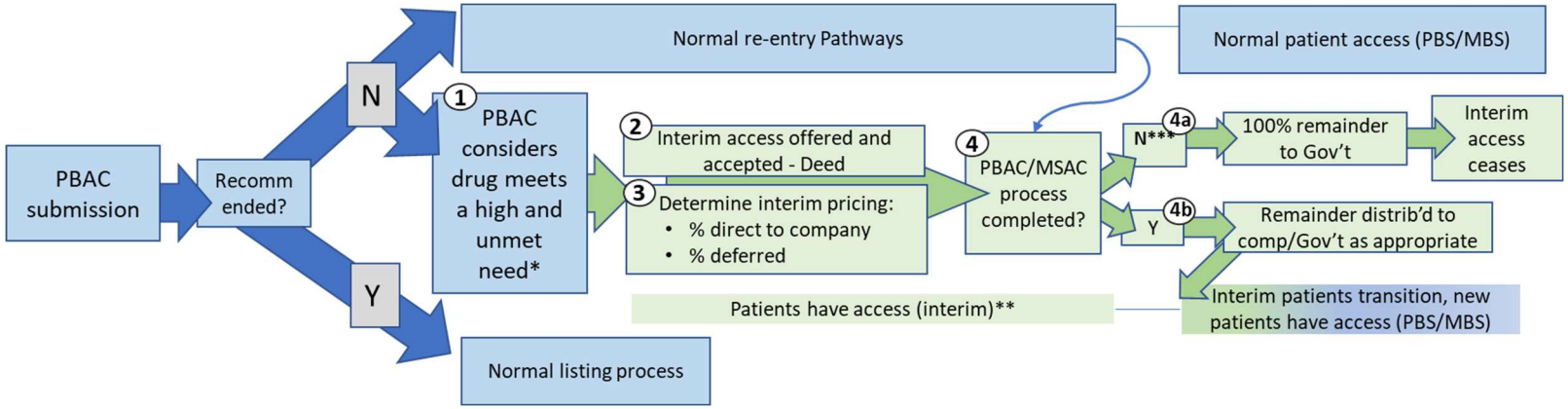
Figure 1 presents a high-level schematic of the existing PBAC/MSAC submission process and how the proposed interim access approach would proceed in parallel. A description of each step of the proposed interim access approach is set out in the text following the figure.

Figure 1 - A schematic illustration of how an interim access approach could be incorporated into the current PBS system

Current PBS system



Proposed interim access approach – Steps of the approach are highlighted in green, and numbered and discussed in the subsequent text



* or: TGA provisional, TGA priority, Orphan, special populations

** Transparency for pts/physicians; ensure no patient disadvantaged (e.g. no forced therapy cessation) regardless of outcome

*** Either the PBS/MBS process not resolved, OR interim access period expires

Step 1 - Options for identifying the health technologies for which the interim access approach could apply

Health technologies for which the interim access approach could apply would be those where the PBAC/MSAC has acknowledged the added therapeutic value of the new technology compared to the alternative, but where for various reasons a recommendation cannot yet be made, AND the company intends to resubmit at the next opportunity, plus at least one of the following:

a) The health technology is for populations which PBAC/MSAC has considered are high need and where this need is unmet.

b) The health technology has been registered via the TGA's priority[10] or provisional[11] registration pathways – i.e. "*…life-threatening or seriously debilitating condition*."

   - Life threatening = "*A condition where the prominent feature (i.e. affecting an important portion of the target population) is serious illness from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of treatment based on mortality and life expectancy data*."[12]
   - Seriously debilitating condition = "*A condition that has as a prominent feature (i.e. affecting an important portion of the target population) which is morbidity with a well-established, major impact on the functioning of the person based on objective and quantifiable medical or epidemiologic information. Short-lived and/or self-limiting morbidity is not considered seriously debilitating.*"[13]

c) It is for a special population (for example, paediatric or indigenous populations).

d) It is for a condition consistent with the TGA's definition of Orphan (**Attachment 2** - Orphan Drug criteria).

Step 2: Options related to the initiation of the interim access process

a) The PBAC could make a recommendation to government that the health technology could be appropriate for interim access (and would indicate a price for the intervention based on its view of the evidence as it stands) – this is the conclusion of the PBAC/MSAC's role in the interim access approach

b) The relevant company would be offered the opportunity to work with government on an interim access approach, and if an agreement is reached (i.e. a Deed is agreed as per below), the interim process would be activated, and patients would have interim access

c) A Deed of Agreement would need to be entered into to set out key aspects of the interim access arrangements (the Department and technology companies are accustomed to this). For example, key elements could include:

   - the interim pricing level - including the direct and deferred components (see Step 3 in Figure 1, and described below);

[10] https://www.tga.gov.au/publication/priority-determination-eligibility-criteria
[11] https://www.tga.gov.au/publication/provisional-determination-eligibility-criteria
[12] https://www.tga.gov.au/acronyms-glossary#id_8769
[13] https://www.tga.gov.au/acronyms-glossary#id_8774

- the duration of the interim access (for example, 12 months. This should be mutually extendable in circumstances where resolution is imminent);
- a mutual commitment to the method of distribution of the deferred pricing component upon cessation of the interim access (either because of the conclusion of the PBS/MBS process, or because of expiry of the interim access period – which also should be agreed within the Deed) (Step 4 in the figure, and described below); and
- the treatment of existing patients in the event of a failure to reach resolution – specifically, for patients who receive the medicine/technology during the interim access period, there should be a commitment to continued supply of the health technology whilst the patient is benefitting (Step 4a in the figure, and described below).

d) Once the Deed is signed, the interim access would need to be activated quickly because any delay equates to a delay in access to the new health technology for patients. It is important to appreciate that at this point in the current PBS/MBS process, the patient does not have access to the new health technology (because a recommendation by PBAC/MSAC has not been achieved).

e) The Medicines Status Website[14] could reflect this situation (e.g. under the heading "PBAC Outcome", wording such as: "Not recommended, interim access being investigated/has been agreed").

Step 3: Options related to establishing the interim access funding level for technology which qualifies for this approach

To reiterate: under this proposal, the usual PBS/MBS process would be unaffected and continue as current in parallel with the interim access approach.

a) The interim funding level would need to comprise a paid component (that the technology company would receive directly) and a deferred component (that would be paid to the company depending on completion of the PBS/MBS listing process which must be proceeding in parallel)

b) The specific approach to establishing the levels of the interim paid and deferred components (but not the final PBS/MBS listing price) could be as follows:

- The paid component - the company would receive this directly, and the price could be consistent with the evidence as it stands, in the view of the PBAC/MSAC.
- The deferred component - the company would not yet receive this, and it would be the difference between the price proposed (requested) by the technology company in its reimbursement submission, and the price consistent with the submission as it stands (in the PBAC/MSAC's view).
- It is extremely important that these pricing levels (both the price proposed by the company, and the price consistent with the submission in PBAC/MSAC's view) remain confidential.

c) The deferred component could be:

[14] https://www.pbs.gov.au/medicinestatus/home.html

- in escrow until the PBS/MBS process has concluded (or until the agreed time period expires) or,
- accounted for in the Deed by setting out an explicit method to calculate the magnitude of the deferred component; for example, based on i) the number of doses (or patients who access the new technology) in the interim period, ii) the direct payment already provided to the company, and iii) the final agreed PBS/MBS pricing.

d) For drug technologies, Special Pricing Arrangements should apply (such that the published price does not equal the agreed price), and wholesaler and pharmacy mark-ups should be applied as normal on the published price.

Step 4: Wrap up of interim access

As described above, the period of interim access should be limited to, for example, 12 months, or until the PBS/MBS process has reached successful conclusion.

The completion of the interim access approach could result in either a transition of the health technology to full PBS/MBS access, or cessation of interim access (with no new patients able to access the reimbursed health technology).

Step 4a) If the PBS/MBS process has not resulted in a pricing agreement, OR if the time period as set out in the Deed has expired, then:

I. Interim funding should cease.

II. No new patients would have reimbursed access to the health technology.

III. Existing patients should continue to have access to the health technology and should not be disadvantaged.

IV. The deferred component of the interim funding could be returned to the government (if it had been in escrow), or otherwise no further payment would be made to the company.

Note that it is possible that in this situation, a resolution to the PBS/MBS process could be achieved at a later date (after cessation of interim access). It would be prudent to ensure that any unpaid deferred payment should be accounted for in any subsequent agreement (PBS/MBS listing Deed). This would be important in order to ensure that technology companies are not disincentivised, or even prevented, from working with government on an interim access approach in the first instance.

Step 4b) If the PBS/MBS process has successfully resolved and a price and listing has been agreed, then:

I. Interim funding should cease.

II. Patients who had accessed the technology during the interim period should have continued access to the PBS/MBS listed technology. One way to ensure a smooth transition is to provide for a Grandfathering clause in the relevant Schedule.

III. The deferred payments (or a proportion) would be paid to the technology company depending on the price justified in the PBAC/MSAC process and agreed with the Minister

This would achieve a very satisfactory outcome for all parties:

- the government will be providing access to an important new health technology at an agreed price,
- the technology company will have achieved reimbursement at an agreed price, and
- most importantly, patients will be able to access the technology up to 12 months earlier than otherwise would have been possible in the absence of interim access.

Conclusion

The present Inquiry represents an opportunity to build upon the excellent work that has previously been undertaken in the TGA and the PBS/MBS processes.

With the inevitable arrival of an increasing number of more specialised health technologies such as gene therapies, and with the potential for increased pricing pressure, it is prudent at this time to understand if there are ways to create a more efficient access system. This is particularly urgent for medicines and technologies which are likely to be advances on existing therapies in areas of high and unmet clinical need.

This submission, which builds on an idea originally raised by the PBAC, proposes a mechanism that could provide early access by Australians to important new medicines and health technologies.

Though there are many details to be identified and addressed, the options provided herein will hopefully stimulate discussion and changes which will help Australians dealing with rare conditions, or where there are few existing options.

Attachment 1 – Comments to Terms of Reference #1, #2 and #3

Term of Reference #1 – The range of new drugs and emerging novel medical technologies in development in Australia and globally, including areas of innovation where there is an interface between drugs and novel therapies

This section talks about the range of medicines and health technologies being developed, the readiness of these to meet the requirements of the Australian system, and a high-level approach to ensuring important medicines are brought to Australia as quickly as possible.

There will be an influx of new medical advances

There are many therapeutic interventions, including gene therapies and co-dependent technologies, being studied in Australia and overseas. The Committee will presumably receive further detail of this from the biotechnology companies and industry bodies which will provide submissions to the Inquiry.

Though obviously not all these interventions will succeed and be registered, many will. According to the Alliance for Regenerative Medicine, there were more than 350 clinical trials in gene therapies (all phases) underway by the end of 2019[15].

It is also likely that many of these will challenge the reimbursement system in Australia. This underscores the importance of the present Inquiry.

Proactively ensure important new advances are brought to Australia in a timely manner

Many companies which are developing valuable new therapies do not have a presence in Australia. It is important that a system be in place to identify such medicines and to engage with these companies in an effort to elevate Australia in the launch plans.

A brief search of online resources demonstrates that there are many companies which have potential medicines for important clinical areas, such as amyotrophic lateral sclerosis (ALS) or Alzheimer's disease, but which do not have a presence in Australia.

Although some companies will enter into commercial arrangements with Australian based companies to bring such medicines to our country, this can be a long process. But if there was a system that identified specific high need conditions, and a process which identified and worked collaboratively with companies which have candidate medicines for these conditions, the process could be expedited.

[15] 111 phase I, 209 phase II, 32 phase III clinical trials with gene therapies end of year 2019: https://alliancerm.org/publication/2019-annual-report/

This could be analogous to AusTrade activities to attract clinical trials to Australia[16], which have been successful[17].

Overall

It is reasonable to expect an influx of new technologies, including gene therapies and co-dependent technology, over the next several years. Many of these will likely represent important advances for patients across a range of areas, including rare and high need conditions. Given the differing regulatory and pricing systems globally, and the potential of expanding international reference pricing discussed earlier[5], Australia should expect that at least some of these costs will challenge the current views on cost-effectiveness. A system should be put in place to proactively identify high need medicines and to work with the relevant company to ensure these are brought to Australia.

Term of Reference #2 – Incentives to research, develop and commercialise new drugs and novel medical technologies for conditions where there is an unmet need, in particular orphan, personalised drugs and off-patent that could be repurposed and used to treat new conditions

This section discusses incentives for technology companies to undertake clinical trials/R&D (with emphasis on local R&D), incentives for companies to pursue re-purposing and commercialisation of off patent medicines and incentives to pursue commercialisation (PBS/MBS reimbursement) of new health technology in Australia.

Re-purposing and commercialisation of off-patent medicines

Reimbursed off-patent medicines, which usually have multiple sponsors, may be registered for a broader range of uses than the reimbursed use, or there may be clinical evidence to support a different non-registered (and thus non-reimbursed) use. In any case, only a few of the sponsor companies will have the willingness, capability and resources to pursue a registration submission, a reimbursement submission, or both.

This means that off-patent medicines, which could be re-purposed for other uses, are likely to not undergo the required steps and so patients will not have access.

There have been examples of off-patent medicines being successfully repurposed (for example, tamoxifen in 2015/2016[18,19]).

[16] "Why Australia for Clinical Trials – National Slide Deck": https://www.austrade.gov.au/ArticleDocuments/6458/Why-Australia-for-Clinical-Trials-Presentation.pdf.aspx
[17] "*R&D incentives attract US oncology drug specialist Moleculin to Australia*": https://www.austrade.gov.au/international/invest/investor-updates/2018/rd-incentives-attract-us-oncology-drug-specialist-moleculin-to-australia
[18] Tamoxifen – AstraZeneca – March 2016: https://www.pbs.gov.au/pbs/industry/listing/elements/pbac-meetings/psd/2016-03/tamoxifen-nolvadex-d-psd-03-2016
[19] https://pharmadispatch.com/news/spittle-the-right-thing-to-do

Consistent with the discussion under ToR#1, one approach may be to identify medicines which can be re-purposed, and to engage with the relevant companies in a collaborative way to secure the required steps (which could comprise a registration step then a reimbursement step).

A further idea could be for government to incentivise companies to proactively seek opportunities for re-purposing by providing other advantages which could be some or more of:

- Tax related
- Exclusivity-related (temporary exclusive TGA and PBS listing)
- Exemption from statutory price impacts.

Clinical trials activity in Australia

The provision of incentives (and removal of dis-incentives) to attract research and development in Australia has been a long-term point of discussion, is a strong focus of Australian government activities (as discussed below in ToR#3) and appears to have been quite successful.

Increased clinical trial activity in Australia provides early access to a technology in a finite window of time, to some people with specific characteristics consistent with trial inclusion criteria, in specific geographical locations (i.e. close to trial centres), and who have well-informed physicians. While clinical trials are critical to achieving access, they themselves should not be considered as acceptable substitutes for broad and equitable patient access, as discussed below (ToR #3).

Commercialisation (pursuit of PBS/MBS reimbursement) in Australia

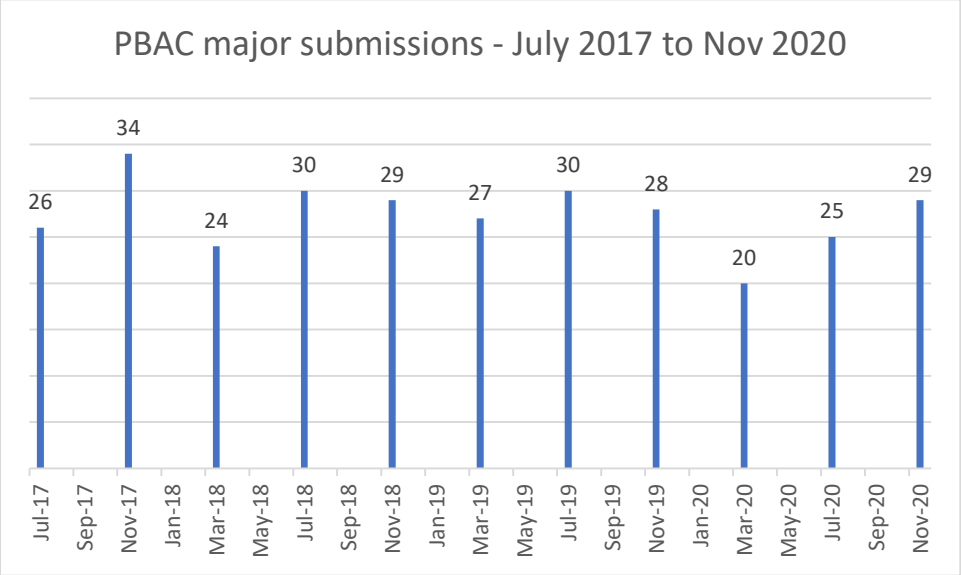
The most important driver of patient access to new health technology in Australia is PBS/MBS reimbursement. This provides ongoing, broad and equitable access to new technology to those who need it, regardless of geographical location and capacity to pay.

If it is accepted that current incentives to commercialise (i.e. pursue PBS and/or MBS reimbursement) are not (or will not be) sufficient, or that there are disincentives to pursue commercialisation, then addressing these would be an important initiative. It will be important to monitor the effect of the previously discussed international reference pricing by the USA[5] on the time to submission of new medicines in Australia.

However, there is no current evidence to suggest that the existing level of incentive (i.e. profitable and viable business environment, and motivation to provide positive patient impact) is insufficient to attract technology companies to submit for TGA registration, and to submit for reimbursement. Submissions for reimbursement appear to be at least at consistent levels[20], (Figure 2) and most medicines which are acknowledged by PBAC to address a high unmet need ultimately achieve reimbursement.

[20] Lybrand, S., Wonder, M. Analysis of PBAC submissions and outcomes for medicines (2010–2018). International Journal of Technology Assessment in Health Care, Volume 36, Issue 3June 2020 , pp. 224-231. https://www.cambridge.org/core/journals/international-journal-of-technology-assessment-in-health-care/article/analysis-of-pbac-submissions-and-outcomes-for-medicines-20102018/50269F447E3F7EF96D0AF8A8F6E78AD5

Figure 2 - The number of major submission (new medicines and new indications) to PBAC – July 2017 to Nov 2020[21]



If any incentive or initiative is to be considered, the aim should be to achieve more rapid patient access to high need health technology. As discussed in ToR#4, one such initiative would require both government and the technology company to find a way to provide access to high need technology while the process of identifying the final agreement on price (i.e. the PBAC/MSAC process) is ongoing.

Term of Reference #3 – Measures that could make Australia a more attractive location for clinical trials for new drugs and novel medical technologies

Any additional measures regarding attracting clinical trial activity should consider, firstly, the current level of government support and, secondly, as discussed above, that clinical trials are not acceptable substitutes for broad and equitable patient access.

<u>For most patients in Australia, clinical trials are not a substitute for equitable access</u>

The Federal Government's Clinical Trial Initiative (which absorbed the Rare Cancers, Rare Diseases and Unmet Clinical Trials initiative[22]), provides $614.2 million over 10 years specifically to increase clinical trial activity. This appears to be a genuine response and investment to attract trial activity to Australia[23]. The initiative is focussed on specific areas: reproductive cancers, childhood brain cancer,

[21] Data sourced from Department of Health Annual Reports https://www.transparency.gov.au/annual-reports/department-health/2018/appendix-2-processes-leading-pbac-consideration-annual-report, and PBAC Agenda documents (https://www.pbs.gov.au/pbs/industry/listing/elements/pbac-meetings/agenda)

[22] https://www.health.gov.au/initiatives-and-programs/rare-cancers-rare-diseases-and-unmet-need-clinical-trials-initiative

[23] "*Clinical Trials Activity initiative. The Clinical Trials Activity initiative helps Australian researchers and patients test new treatments through national and international clinical trials*" https://www.health.gov.au/initiatives-and-programs/clinical-trials-activity-initiative

neurological disorders, low-survival cancers and diseases, and international clinical trial collaborations.

Trial activity overall is occurring in Australia - according to the Australia and New Zealand Clinical Trials Registry (ANZCTR), as of 23 September 2020, there are 544 phase 3, and 82 phase 2/3 intervention trials recruiting or active in this country[24].

Clinical trials are critical to understand and support (or not) the registration of new technology. Clinical trials do provide early access to new technology, while the trial is running, for some people who fulfil trial eligibility criteria, who live in the right geographical location and whose physician is aware of, or seeks out, the trial.

In the context of aiming to achieve equitable patient access to important new technologies, it must be appreciated that clinical trials do not themselves equate to equitable national access. They are not an acceptable substitute for access on the Pharmaceutical Benefits Scheme (PBS) or the Medicare Benefits Schedule (MBS). As mentioned previously, the most important driver of patient access to new health technology in Australia is PBS/MBS reimbursement, which provides ongoing, broad and equitable access to new technology to those who need it, regardless of geographical location and capacity to pay.

[24] ANZCTR (accessed 23 September 2020): https://www.anzctr.org.au/TrialSearch.aspx#&&conditionCode=&dateOfRegistrationFrom=&interventionDescription=&interventionCodeOperator=OR&primarySponsorType=&gender=&distance=&postcode=&pageSize=20&ageGroup=&recruitmentCountryOperator=OR&recruitmentRegion=&ethicsReview=&countryOfRecruitment=Australia%7cNew+Zealand&registry=&searchTxt=&studyType=&allocationToIntervention=&dateOfRegistrationTo=&recruitmentStatus=Recruiting&interventionCode=Treatment%3a+Drugs%7cTreatment%3a+Surgery%7cTreatment%3a+Devices&healthCondition=&healthyVolunteers=&page=1&conditionCategory=&fundingSource=&trialStartDateTo=&trialStartDateFrom=&phase=Phase+3

Attachment 2 - Orphan Drug criteria

(from Section 16J of the Therapeutic Goods Regulations 1990[25])

16J Designation of medicine as orphan drug

(1) On receiving an application under subregulation 16H(1) to designate a medicine as an orphan drug, the Secretary must:

(a) consider the application; and

(b) decide either:

(i) to designate the medicine as an orphan drug; or

(ii) to refuse to designate the medicine as an orphan drug.

(2) The Secretary may decide to designate the medicine as an orphan drug if the Secretary is satisfied, having regard to any matter that the Secretary considers relevant, that:

(a) if the medicine is not a new dosage form medicine—all of the criteria specified in subregulation (3) are satisfied in relation to the medicine; or

(b) if the medicine is a new dosage form medicine—all of the criteria specified in subregulation (4) are satisfied in relation to the medicine.

General criteria

(3) The following criteria are specified in relation to a medicine that is not a new dosage form medicine:

(a) the application is for only one indication of the medicine;

(b) the indication is the treatment, prevention or diagnosis of a life-threatening or seriously debilitating condition in a particular class of patients (the ***relevant patient class***);

(c) it is not medically plausible that the medicine could effectively treat, prevent or diagnose the condition in another class of patients that is not covered by the relevant patient class;

(d) at least one of the following applies:

(i) if the medicine is intended to treat the condition—the condition affects fewer than 5 in 10,000 individuals in Australia when the application is made;

(ii) if the medicine is intended to prevent or diagnose the condition—the medicine, if it were included in the Register, would not be likely to be supplied to more than 5 in 10,000 individuals in Australia during each year that it is included in the Register;

(iii) it is not likely to be financially viable for the sponsor to market the medicine in Australia unless each fee referred to in paragraph 45(12)(c) were waived in relation to the medicine;

(e) none of the following has refused to approve the medicine for the treatment, prevention or diagnosis of the condition for a reason relating to the medicine's safety:

[25] https://www.legislation.gov.au/Details/F2020C00762

(i) the Secretary;
(ii) the United States Food and Drug Administration;
(iii) the European Medicines Agency;
(iv) Health Canada;
(v) the Medicines and Healthcare products Regulatory Agency of the United Kingdom;

(f) either:
(i) no therapeutic goods that are intended to treat, prevent or diagnose the condition are included in the Register (except in the part of the Register for goods known as provisionally registered goods); or
(ii) if one or more therapeutic goods that are intended to treat, prevent or diagnose the condition are included in the Register (except in the part of the Register for goods known as provisionally registered goods)—the medicine provides a significant benefit in relation to the efficacy or safety of the treatment, prevention or diagnosis of the condition, or a major contribution to patient care, compared to those goods.

New dosage form medicines

(4) The following criteria are specified in relation to a new dosage form medicine:
(a) the application is for only one indication of the medicine;
(b) the indication is the treatment, prevention or diagnosis of a life-threatening or seriously debilitating condition;
(c) it is not likely to be financially viable for the sponsor to market the medicine in Australia unless each fee referred to in paragraph 45(12)(c) were waived in relation to the medicine;
(d) none of the following has refused to approve the medicine for the treatment, prevention or diagnosis of the condition for a reason relating to the medicine's safety:
(i) the Secretary;
(ii) the United States Food and Drug Administration;
(iii) the European Medicines Agency;
(iv) Health Canada;
(v) the Medicines and Healthcare products Regulatory Agency of the United Kingdom;
(e) either:
(i) no therapeutic goods that are intended to treat, prevent or diagnose the condition are included in the Register (except in the part of the Register for goods known as provisionally registered goods); or
(ii) if one or more therapeutic goods that are intended to treat, prevent or diagnose the condition are included in the Register (except in the part of the Register for goods known as provisionally registered goods)—the medicine provides a significant benefit in relation to the efficacy or safety of the treatment, prevention or diagnosis of the condition, or a major contribution to patient care, compared to those goods.

Publication of decision

(5) If the Secretary decides to designate the medicine as an orphan drug, the Secretary must, as soon as practicable after making the decision, publish a notice on the Department's website stating the following:

(a) the name of the sponsor of the medicine;

(b) the indication referred to in paragraph (3)(a) or (4)(a);

(c) the dosage form of the medicine;

(d) that the medicine is a designated orphan drug.

Notification of decision

(6) As soon as practicable after making the decision, the Secretary must notify the applicant, in writing, of the decision.

(7) If the Secretary decides to refuse to make the designation, the notification must include the reasons for the decision.