House of Representatives Standing Committee on Health, Aged Care and Sport inquiry into approval processes for new drugs and novel medical technologies in Australia

Submission from Medicines Australia

November 2020

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PART 1: MEDICINES AUSTRALIA SUBMISSION TO THE PARLIAMENTARY INQUIRY INTO APPROVAL PROCESSES FOR NEW DRUGS AND NOVEL MEDICAL TECHNOLOGIES IN AUSTRALIA

Introduction

Medicines Australia is the peak body representing the innovative, research-based, medicines industry in Australia. Our members develop, manufacture, and supply critical medicines and vaccines available on the pharmaceutical benefits scheme (PBS) and the national immunisation program (NIP). Our membership comprises small, medium, and large Australian and multi-national companies. Many of the world's multi-national medicines manufacturers are members of Medicines Australia through their local affiliates. These local affiliates provide a critical worldwide connection that enables Australians to access globally developed breakthrough medicines and therapies.

Part 1 of this submission focusses on four key themes directly relevant to the Inquiry's Terms of Reference and makes recommendations to enhance Australia's evaluation and approval processes for new drugs and novel technologies and to expand the medicines access and eco-system to contribute to Australia's economic security. Part 1 also includes some background supporting information and case studies.

Part 2 of the submission addresses the specific Terms of Reference to the Inquiry with further detail that builds on Part 1 and the recommendations.

Executive Summary

As the representative industry body for the innovative, research-based, pharmaceutical sector in Australia, Medicines Australia provides strong support to Australia's national public health initiatives through Medicare, the PBS and MBS, the NIP and State and Territory health authorities.[1]

The COVID-19 pandemic has unquestionably established that Australia's overall health and economic indicators are inextricably linked. Medicines are an integral component of healthcare and assist Australians to live longer and healthier lives, remain productive and employed, avoid hospitalisation, and positively participate in, and contribute to, the community and the economy. Every innovative medicine made available in Australia generates a significant return on investment to the patient, the community, the economy, and the Government.[2]

Advancements in scientific research and development, coupled with the pace of change in technology, are shifting the approaches to disease definition, development of medicines, and the prescribed treatments. This is highlighted by the intended objective of personalised (or precision) medicine. The objective of personalised medicine is to utilise individual molecular diagnostic tests and targeted therapies to get the right treatment to the right patient at the right dose the first time.

The breadth and complexity of new and emerging medicines, through advancements in technology and scientific research and development, is not without challenges. Particular challenges in Australia are found in the regulatory and reimbursement assessments of technical criteria (and outcomes of those assessments), which are not synchronised, nor even roughly aligned, with the speed of innovation and the evolution of medicines. As a consequence, these challenges impact the time it takes to bring the benefits of innovation in medicines, therapies, and vaccines, to deserving Australian patients.

Medicines Australia's submission to this Inquiry focuses on four pillars.

1. Timeliness of access to new medicines through Australia's regulatory and reimbursement processes.
2. Research and development, including clinical trials.
3. The role of the consumer in medicines access.
4. The global context to the regulatory and reimbursement environment.

[1] Pharmaceutical Benefits Scheme (PBS); Medicare Benefits Scheme (MBS); National Immunisation Program (NIP)
[2] https://medicinesaustralia.com.au/medicines-matter-an-investment-for-a-healthier-tomorrow/

1. Timeliness of access to new medicines (regulatory and reimbursement)

With the introduction of Health Technology Assessment (HTA)[3] in 1992, Australia led the work in introducing many major therapeutic advances. These advances brought dramatic shifts in life expectancy and quality of life to those with HIV, cancer, hepatitis, and many chronic diseases. However, HTA has not evolved as rapidly as advancements in scientific research and technological developments. Medicines Australia argues that Australia is no longer at the forefront of medicines access. There are numerous examples of medicines taking extensive periods, in some cases years, for entry onto the PBS. Overall, the systems and processes designed to support medicines access do not universally do so. Medicines Australia submits to the Inquiry, recommendations that will reform and resolve the process, so that it is contemporary and fit for purpose into the future.

If Australia aspires to be at the forefront of healthcare, compared against leading international benchmarks, these process delays need to be resolved as a priority. Two key areas that enable access to new medicines in Australia are the process for registering a product for marketing in Australia (regulatory); and the process to achieve government subsidy (reimbursement). The regulatory and reimbursement processes are the prerequisite following the culmination of discovery, research, and clinical and non-clinical evidence development that underpins the decision making. For this reason, Medicines Australia's submission will identify issues and make practical recommendations for each of the key areas, and against the terms of reference for the Inquiry.

2. Research and development, including clinical trials

In addition to ensuring the regulatory and reimbursement systems are future proofed for early access to innovative medicines and treatments, Australia also needs to reassert a place at the forefront of major innovation for pharmaceutical *discoveries*. Reinforcing our existing strengths, that underpin Australia's capacity and capability in research and development (R&D), and improving policy vulnerabilities around intellectual property (IP), will be key to securing the early discovery and pipeline development for new, innovative, and advanced therapies in Australia.

Research and development through to commercialisation, in the innovative pharmaceutical industry, is part of a global network, where there is growing international competition. Therefore, incentivising the ecosystem to support partnerships and collaborations will help to bolster Australia's position when competing globally for investment.

Clinical research trials are the pivotal phases of R&D that require specific focus. Clinical trial activities can be conducted anywhere, including outside Australia. The new knowledge gained from conducting clinical trials in Australia has a wider Australian economic benefit. That is, clinical trials deliver measurable, tangible, health benefits to Australian patients and spill over benefits to the broader economy through knowledge development and jobs creation. In this way clinical trials provide benefits to Australian patients, the overall healthcare system, the broader medical research industry, and the Australian economy.

Australia currently holds a strong international reputation as a location for high quality clinical trials. However, sustaining this reputation is increasingly challenging, as international competition for the placement of clinical trials has already begun to erode Australia's advantage. Rather than relying on historical recognition as a reliable destination for quality clinical research, Australia needs to actively demonstrate superiority against other international benchmarks in clinical trials, to secure status as a preferred destination of choice.

Improvements such as time to initiation and pace of recruitment are necessary. Resolving some long-standing regulatory and governance issues would speed up trial initiation processes and help to improve Australia's capacity to attract more clinical trials. A goal to double Australia's clinical trial activity,

[3] Health Technology Assessment (HTA) is the systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies.

and expand clinical trial access to regional areas, would generate economic activity and support economic and health recovery. Additionally, recently announced changes to the Research and Development Tax Incentive (RDTI) should be evaluated to ensure that barriers have not been inadvertently introduced and that local and global pharmaceutical companies continue to invest in clinical trials within Australia, as this investment can be a key driver of economic growth.

3. The role of the consumer in medicines access

Our existing Health Technology Assessment system currently lacks adequate mechanisms to consistently recognise value and include in the decision making the unique information patients have about a condition and its impacts. There remains significant scope for continued evaluation and improvement in the contribution and participation of consumers and patients into HTA, as highlighted in a range of submissions already made to this inquiry.[4] This input should extend both specifically from a single treatment or medicine, and to the health system more broadly.

The system should enable consumers and patients to contribute to the decisions for access to medicines and therapies made available through Australia's Medicare, MBS, and PBS systems, including input to the decision makers about the reimbursement of individual medicines. Such input might assist improved valuation of patient and community benefit:

4. The global context to the regulatory and reimbursement environment

Medicines research, development, manufacture, and supply are conducted globally and will only increase with further globalisation. This means that the market in Australia cannot, and does not, operate in isolation from the rest of the world.

Global approaches are often applied to the medicines research, development, and market authorisation processes, as seen with trends towards globally harmonised regulatory systems,[5] and work-sharing across international regulatory authorities[6]. The frequency of this kind of global cooperation is increasing. Additionally, the maturity and sophistication of regulatory agencies can influence global company decisions on where to launch innovative medicines first. Medicines companies find it easier to accelerate timeliness for medicines' launch when there is a high level of global harmonisation.

Australia's position as a "first wave" country for registration and reimbursement of medicines is at risk, particularly where the Australian system may not have adequately considered the global context, and unintended consequences to global investment, when implementing local policy decisions. However, there are a range of improvements to Australia's regulatory and reimbursement system, which Australia could implement, to ensure we strengthen our "first wave" status and ensure Australian patients get early access to the latest therapeutic innovations.

Over several years the medicines industry has worked with the government to modernise and speed up decision making processes. For example, with the introduction of 'Parallel TGA and PBAC' evaluations.[7] Nevertheless, Australia's current HTA process continues to present global and local delays to medicines access, which intensifies as we endeavour to navigate newly evolving treatments and rare diseases without clarity of process or transparency of funding models.

[4] Inquiry into approval processes for new drugs and novel medical technologies in Australia, https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/Newdrugs/Submissions

[5] The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), https://www.ich.org/

[6] Work sharing initiative through the Access Consortium, including Therapeutic Goods Administration (TGA), Health Canada (HC), Singapore's Health Sciences Authority (HSA), the Swiss Agency for Therapeutic Products (Swissmedic) and UK Medicines and Healthcare products Regulatory Agency (MHRA), to maximise international cooperation, reduce duplication, and increase each agency's capacity to ensure consumers have timely access to high quality, safe and effective therapeutic products. https://www.tga.gov.au/australia-canada-singapore-switzerland-united-kingdom-access-consortium

[7] https://www.pbs.gov.au/info/publication/factsheets/shared/tga-pbac-parallel-process

Recommendations

1. Timeliness of access to new medicines (regulatory & reimbursement)

Efficient and globally competitive access to new medicines, therapies and vaccines in Australia can be continuously improved through progressive improvements to Australia's regulatory and reimbursement processes that reinforce Australia's position as a "first wave" launch country for new medicines and therapeutics.

Regulatory recommendations (TOR 4):

1. Streamline evaluation process across all independent and government advisory bodies involved in review of new medicines and technologies, where possible.
2. Enable a joint Therapeutic Goods Administration (TGA); Pharmaceutical Benefits Advisory Committee (PBAC); Medical Services Advisory Committee (MSAC), Australian Technical Advisory Group on Immunisation (ATAGI) pre-submission advice framework to improve alignment of end-to-end processes.
3. Update TGA regulatory processes to include *expedited* pathways for cell therapies that mirror pathways for prescription medicines, such as *priority review and provisional determination*
4. Introduce statutory 30-day review timeframes and monitoring mechanisms for CTX review

Reimbursement recommendations (TOR 4):

1. Modernise and improve HTA evaluation processes in line with international best practice HTA and better capture the impact of the social and economic contribution of medicines, such as patient reported outcomes, productivity and community
2. Ensure consistency and alignment across all HTA processes
3. Work with industry to establish and introduce flexible and adaptable assessment models and funding mechanisms which recognise innovation and for new technologies where there are no current agreed/defined pathways.
4. Enable consumers, patients, and patient groups to provide timely and relevant input to the decision-making process for individual technologies through patient led initiatives.
5. Establish a new oversight committee to provide independent supervision of the post-PBAC price negotiation process between industry and government and ensure appropriate risk sharing is put in place.
6. Reinstate annual dialogue between industry (represented by Medicines Australia) and the PBAC to consider and create opportunities to resolve issues of relevance for a contemporary HTA process

2. Research and development, including clinical trials

Incentives for businesses to make additional investments in research and development, clinical trials and commercialisation are key to economic recovery and growth and are based on stable, predictable and focused tax incentives; strong and reliable Intellectual Property protections; more efficient clinical trials environment; enhancing commercialisation opportunities and a better skilled and experienced domestic and migrant workforce.

Research and development recommendations (TOR 2):

1. Work with industry to review the impact of the revised Research and Development Tax Incentive (RDTI) on pharmaceutical innovation, clinical trials, and innovative manufacturing to identify if further changes are warranted.
2. Consider potential for the Medical Research Future Fund (MRFF) to be linked or mirrored to the EU's Horizon Europe project.

Clinical Trial recommendations (TOR 3):

1. Update public health policies to provide that the following are mutually accepted by all States, Territories and universities participating in a clinical trial.
2. Harmonise Human Research Ethics Committee (HREC) and Site-Specific Assessment (SSA) submissions into one Australian online platform; and enable parallel review by HRECs and Research Governance Offices (RGO).[8] The platform should be developed within the purview of the Australian Commission on Safety in Healthcare (ACSQH).
3. Develop and launch a National Community Awareness Campaign for Clinical Trials.
4. In consultation with industry, invest in and develop a national standard approach, including nationally agreed systems and standard operating procedures to support and strengthen the capacity to conduct clinical tele-trials in rural, remote, and regional areas, and including regional tele-trials in community awareness campaigns.
5. Invest in and adopt modernised digital technologies and practices to position Australia as the premier destination for international clinical trials.

3. The role of the consumer in medicines access

Health technology assessments have increased in scale and complexity making them less accessible for the patient. Whilst those patients that have access to a group, association, or patient organisation, have a path to develop an aligned and coordinated approach to participation, for patients with less common conditions, this opportunity may not exist. Developing a variety of mechanisms to allow for all patient inputs (including voice, video, written) and ensure all individuals with varying levels of resources, capacity and health literacy, as well as individuals living with disability, have equal opportunity to contribute, will improve decision making.

Consumer and stakeholder recommendations (TOR 4):

1. Expanded stakeholder involvement in decision making; before, during and after HTA consideration, should be factored into an improved process, including improvements to opportunities for public consultation and stakeholder research.
2. Strengthen Consumers voice in the healthcare system to contribute to the decisions for access to medicines and therapies, including input to the decision makers about the reimbursement of individual medicines. Such input might assist improved valuation of patient and community benefit:
   - build capacity to engage, improve understandable feedback for consumers, and ensure there is equal and consistent opportunity for all consumers to contribute to the HTA process.
   - improve patient input processes to ensure the Australian healthcare system sets the needs, values, and expectations of those who most depend on it.
   - enable consistent inclusion of Patient Reported Outcome Measures (PROMs).

[8] For example, developed under the remit of the Australian Commission on Safety and Quality in Healthcare.

Background Supporting Information and Case Studies

1. Timeliness of access to new medicines

Monumental shifts in the way diseases will be treated are now taking place. Advancements in scientific research and development, coupled with the rate of change in technology, are changing the approaches to disease definition, development of medicines and the prescribed treatments. This is highlighted by the intended objective of what is referred to as personalised medicine, or precision medicine. The objective of personalised (precision) medicine is to utilise molecular diagnostic tests and targeted therapies to get the right treatment to the right patient at the right dose the first time.

Pharmaceutical companies represented by Medicines Australia have a broad and deep pipeline of innovative or advanced therapy medicinal products (ATMPs) including Gene Therapy Medicinal Products (GTMP) in cell therapies; and biomarker selected therapies (non-ATMPs requiring a diagnostic). New therapies will also make use of advances in digital technologies such as Artificial Intelligence, machine learning and advanced analytical capabilities. Australia has led the world in introducing many major therapeutic advances which have brought dramatic shifts in life expectancy and quality of life to those with HIV, cancer, hepatitis and other acute and chronic diseases.

The breath and complexity of new and emerging medicines, through advancements in technology and scientific research and development, is not without challenges. Such challenges are regulatory and reimbursement assessments of a technical criteria which are in no way synchronised, or even roughly aligned, with the speed of innovation and the evolution of medicines. As a consequence, these challenges impact the time it takes to bring the benefits of innovations to medicines, therapies, and vaccines to deserving Australian patients.

The two key areas that enable access to new medicines in Australia are the process for registering a product for marketing in Australia (regulatory); and the process to achieve government subsidy (reimbursement).

In terms of registration, the pharmaceutical manufacturer of a new medicine (the sponsor) applies to the Therapeutic Goods Administration (TGA) for registration of a medicine. This is also referred to as market authorisation. The TGA undertakes a thorough assessment of the data collected through years of the medicine's development program to determine its suitability (quality, safety and efficacy) for entry on the Australian Register of Therapeutic Goods and thus marketing in Australia.

In terms of reimbursement, before any patient can gain subsidised access to a new medicine in Australia, the medicine has to be made available (listed) on the Schedule of Pharmaceutical Benefits through the PBS. To list on the PBS requires a positive recommendation from the Pharmaceutical Benefits Advisory Committee (PBAC) after it has considered an application, most commonly from the sponsor. The HTA process by which a sponsor seeks reimbursement is fully described in the Department of Health's website. The PBAC reviews follow a fixed 17-week cycle, three times per year. The full process, from submission to publication of public summary document, takes 33-35 weeks (or up to 43 weeks for a co-dependent submission) and does not include other listing requirements.

Current and former PBAC Chairs have cited this as the fastest reimbursement process in the world. However, practical experience shows that very few medicines evaluated for cost-effectiveness receive a positive recommendation in the 17 weeks from their first submission. Most medicines and applications for new indications require more than one submission to achieve a positive PBAC recommendation and subsequent PBS listing.

To prepare and resubmit, following an initial rejection, takes at least one and sometimes more cycle(s). It commonly takes 12 to 18 months for a positive decision and can take several years in some instances. This is a key factor in the time lag from TGA approval to PBS listing.

A study by Lybrand and Wonder (2020)[9] looking at PBAC outcomes found that it took, on average, 1.70 submissions that included a full economic evaluation of any type, to obtain a PBAC recommendation. It took more submissions to obtain a PBAC recommendation for a submission with a cost effectiveness analysis (CEA) (2.35) than it did for a submission with a cost minimisation analysis (CMA) (1.38) (Table:1)

Table1: Number of submissions required to obtain a PBAC Recommendation

Category	Submission attempts (n)	Recommendations (n)	Average number of submission attempts
All	875	514	1.70
CEA	405	172	2.35
CCA[a]	5	4	1.25
CMA	369	268	1.38
CA[b]	14	11	1.27
Not required	68	50	1.36
Not available[c]	7	4	1.75
Unknown[d]	7	5	1.40

[a] Cost consequence analysis
[b] Cost analysis
[c] An economic evaluation was not included in the submission but should have been
[d] Unknown because there is no PSD

For many years since the 1990s Australia was regarded as a leader in the field of health technology assessment. Medicines Australia argues that Australia is no longer at the forefront of medicines access. This fall is due to a combination of factors such as the HTA system, the breath of the value consideration, or other funding constraints. The systems and processes designed to support access are not universally doing so to achieve the medicine access objective.

Medicines Australia considers that the timeliness for medicines access in Australia today is not comparable to that expected of a world leading system. Nevertheless, there are some positive initiatives.

a. There is an increasing number of patients accessing world-leading clinical trials, which allow for earlier access to the latest innovations.
b. There are reductions in time to regulatory filing in Australia, as a result of reforms to the regulatory pathways.
c. The parallel processing of regulatory and reimbursement processes has meant earlier consideration of some reimbursement applications.

Despite these positive initiatives, however, it is Medicines Australia submission that actual universal medicines access is lagging behind comparable countries that we benchmark against. For example, in Australia 60 percent of new medicines achieve reimbursement within 12 months; while in Japan, Germany, and Austria, 60 percent of new medicines achieve reimbursement within 3 months.

As at the end of 2019, there are 96 new medicines that have been registered in Australia, that have not achieved PBS listing.

[9] S Lybrand and M Wonder "Analysis of PBAC submissions and outcomes for medicines (2010-2018)" International Journal of Technology Assessment in Healthcare 1-8, June 2020

The access experience in Australia.

PRIORITY REGISTRATION PATHWAYS

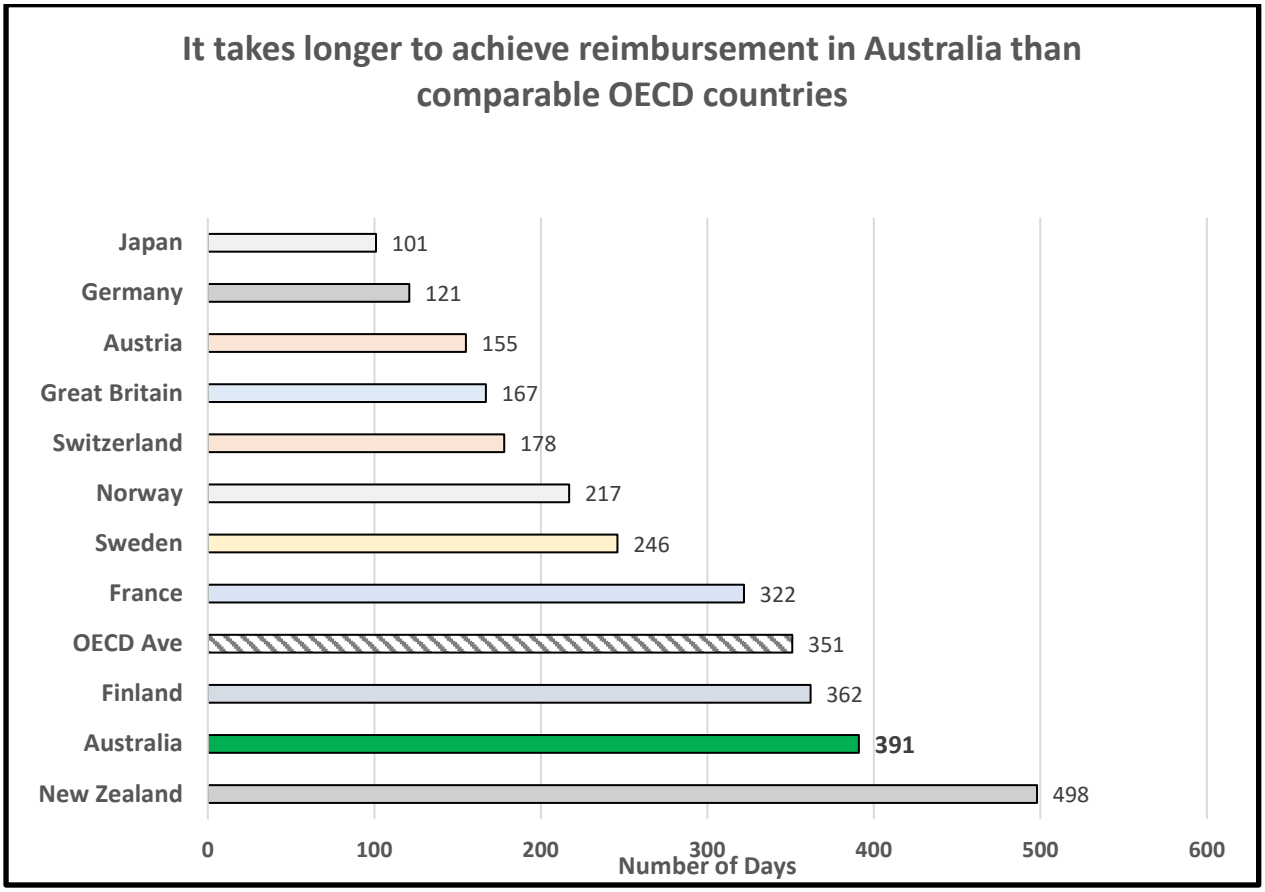
Priority Registration Pathways have seen improvements in the TGA registration times. During 2018 and 2019 six medicines went through the Priority Review Pathway, and on average they were processed 182 days quicker than medicines on the standard review pathway. However, of the six medicines which have been approved for this pathway, none have yet been listed on the PBS (As of December 2019).

TIMEFRAMES FROM REGISTRATION TO REIMBURSEMENT ARE IMPROVING

Timeframes have been improving, however there is room for further improvement when relative OECD markets are considered. In Australia, 60 percent of new medicines achieve reimbursement within 12 months, while in Japan, Germany, and Austria, 60 percent of new medicines achieve reimbursement within 3 months (Figure:1).

Most new medicines are oncology products, and these have some of the longest listing times. There were fewer oncology products listed in 2019 compared to previous years, and this coincides with the high PBAC rejection rate for these products in that year.

Figure 1: Average number of days to achieve PBS listing10



Medicines Australia's strong contention in this submission is that improvements to timeliness of medicines access will most likely have the single biggest impact towards meeting consumer expectations in relation to their healthcare needs.

[10] Medicines Matter: forthcoming publication by Medicines Australia

Urgent and important gaps identified in access to new medicines

There are urgent and important gaps in medicines access for some populations, sub-populations, and for certain conditions such as rare cancers. Populations for which there is limited evidence are under-served by the usual development process, requiring flexibility in development approach, evidence generation and evidence evaluation. This includes the use of real-world data in support of utilisation, where clinical trials are not available. Medicines Australia argues there is insufficient flexibility in the system to address these issues and that these gaps will continue to permeate perceptions of medicines access.

The system also lacks adequate methodologies to enable appropriate access to combination treatments. Evolution in treatment options has led to the increased use of combination therapies, (two or more treatments delivered in parallel or synergistically) that provide valuable incremental benefits to patients. However, the benefits are inadequately valued, and it is increasingly difficult to achieve implementable terms for listing combination therapies or combination treatment regimes. Recent attempts to examine and resolve this ongoing concern have made little progress.[11]

Another gap in access relates to new types of medicines that require specific expertise, infrastructure or adjusted processes to achieve access. Examples include those in the cell and gene therapy space, where larger overseas biotechnology companies without a presence in Australia experience barriers to entering this market, or delay entry and filing registration due to uncertainty or factors related to the small size of the Australian market.

Funding and pricing considerations linked to access to new medicines

Achieving subsidised access in Australia is becoming increasing difficult for a number of reasons.

a. The way in which medicines are valued through the HTA process excludes or inadequately considers key additional or spill over benefits delivered by a medicine or combination of medicines, with the immediate cost being the main consideration rather than long-term benefits.
b. This makes it harder to achieve the required cost effectiveness sought by the PBAC.
c. In turn, pricing becomes a major challenge for companies and in particular, the ability to secure a fair return for the medicine in a way that is globally competitive and/or reasonably consistent.
d. The use of arrangements that cap expenditure on an individual therapy counters the premise of cost effectiveness in the context of an uncapped PBS and the ongoing Government commitment to list all medicines recommended by the PBAC.
e. The focus on total cost of a listing, used as a weapon in negotiations, ultimately undermines the cost effectiveness approach that Australia celebrates, and in turn may lead to a breakdown in discussions and agreements, with resultant gaps in access.

This issue causes the greatest strain in the ability to achieve subsidised access for Australian patients.

The role of clinical trials (and compassionate supply) in delivering early access to new medicines

There is high demand, and high consumer expectation, for access through other means while the processes of regulatory and reimbursement are navigated. Industry responds, although not in all circumstances, in three crucial ways.

a. Through compassionate access provisions, in which companies may provide the medicine before regulatory approval on compassionate grounds to individual patients. This is wholly reliant on the company, usually the local company, to navigate the required internal processes and secure supply, and this can be very challenging to achieve.
b. Through clinical trials conducted in Australia. This provides rich opportunities for collaboration and partnerships. Australia has done well to capitalise and build its clinical trials capabilities. Medicines Australia is a significant advocate for continuing to build clinical trials capabilities.

[11] "Assessing and Evaluating Combination Medicines", a whitepaper, commissioned by Medicines Australia and prepared by SYNEVi Pty Limited, August 2019 and an international scientific congress hosted by Bellberry Limited entitled "Challenges of Valuing and Paying for Combination Therapies in Oncology" was held in November 2019. Publications available on request.

c. In the period between regulatory approval and universal access through the PBS/MBS, there may be high consumer and clinical demand for access. Where there is high need, many companies have sought to accommodate this expectation through pre-PBS programs to allow access.

These three circumstances for early access rely on sufficient confidence that the medicine will be able to secure PBS listing and hence, subsidised access for Australian patients.

2. Research and development, including clinical trials

Successful innovation incentives are founded on creating a sustainable and growing ecosystem of domestic and international partnerships for research and development and subsequent commercialisation. This also opens advanced manufacturing and export opportunities. R&D is key. Trusted partnerships are essential. The COVID-19 pandemic has reinforced that a global problem needs a globally supported solution. One of the Australian pharmaceutical industry's roles during the pandemic has been to contribute to international research and development efforts in developing diagnostics, treatments, and vaccines.

Incentivising an eco-system of partnerships for research and development through to commercialisation in the innovative pharmaceutical industry must be underpinned by recognition that Australia is part of a growing global network. A network in which Australia can play a leading global and, especially, regional role. As discussed in TOR2, Australia can better incentivise the pharmaceutical sector through:

- stable, predictable, and focused tax incentives.
- strong and reliable Intellectual Property protections.
- a more efficient clinical trials environment (see Term of Reference 3: Clinical Trials).
- enhancing commercialisation opportunities.
- a better skilled and experienced domestic and migrant workforce.

While it is difficult to quantify the value of potential growth in research and development and commercialisation, it is worth highlighting that Australian pharmaceutical company research and development spend of $1.5 billion[12] in 2018 is approximately 0.85% of world total expenditure, which stood at 172 billion,[13] and which may be even higher. This investment has the potential to grow, should Australia's policy approaches be amended to align with global best practice.

Clinical trials provide measurable health gains to Australian patients, generate new knowledge for a learning healthcare system, and provide spill over benefits to the broader medical research industry and to the Australian economy. Australia currently holds a strong international reputation as a location for high quality clinical trials. Sustaining our success will be a challenge as international competition for the placement of clinical trials has already begun to erode Australia's historical advantages.

In 2019, there were 1,820 ongoing trials in Australia: a 22% increase on 2015. This contributes an estimated $1.1 billion a year to the economy. This figure could easily be doubled over the next 5 years by industry working with governments to create the right settings to realise this ambition.

In order to remain a world leader in the delivery of clinical trials, and to attract more clinical trials to Australia, we must be able to:

1. commence trials quickly and in a consistent, harmonised, and efficient manner across multiple centres around Australia.
2. Increase the ability for patients to participate in clinical trials. In particular, ensure there is wide recognition and equitable access to clinical trials for patients located in regional areas, through building tele-trials capabilities. This will ensure that clinical trials recruitment is similar to, or greater than that seen in other countries.
3. Adopt modern and future-ready technologies to enable clinical trial processes to be conducted efficiently, cost-effectively, and where possible, remotely.

[12] https://www.mtpconnect.org.au/images/2019%20MTPConnect%20Sector%20Competitiveness%20Plan.pdf
[13] https://www.evaluate.com/sites/default/files/media/download-files/WP2018.pdf

3. The role of consumers in medicines access

Australians' expectations of their healthcare needs are rising significantly. Australians expect improvements in their individual and family's healthcare over the long-term. They are also more aware of international advances and want to be actively involved in decisions affecting their health.

In recent years there has been positive progress concerning the involvement of consumers in HTA decision making. Medicines Australia acknowledges the progress that has been made to better involve Australian patients in approval and reimbursement processes for health technologies, especially through the formation of the Patient Evidence and Engagement Unit in the Office of Health Technology Assessment in 2019.

However, researchers and policymakers overlook critical issues when striving to improve health outcomes because they lack essential contextual knowledge which patients gain from living with a condition or using a treatment. Meaningful patient involvement can address this gap. Current HTA review systems lack the mechanisms to fully recognise, and value, the unique information patients have about a condition and its impacts, including the social value of treatments. Understanding and taking account of patient input and patient-based evidence related to non-health factors that are important to patients should be formalised. Such as, impacts on income generation, social responsibilities and social wellbeing including survivorship, which are essential for patients and demonstrate the additional, important impacts of using a medicine.

Equal and consistent opportunities for consumers to contribute to the HTA process to provide these experiences and evidence, can be further improved. Patients should be able to engage before, during and after HTA consideration, for example from scoping to feedback, and allowing patients or patient groups' involvement in Committees like DUSC and ESC. Such input might address gaps and uncertainties of Committee members, for example, regarding trade-offs that different patients will make. This is especially important for rural and remote patients who may in some cases not be realising the benefits of innovative healthcare because their setting has not been properly understood.

In addition, Medicines Australia would like to continue working with the Department of Health, Technology Assessment and Access Division, to explore mechanisms to allow pharmaceutical sponsors to provide a plain language half page summary of their submission, to be made accessible to consumers, similar to the Scottish Health Technologies Group Plain language summaries.

Enhanced patient involvement in the processes supporting medicine assessment and evaluation will ensure the Australian healthcare system is enhanced to meet the needs, values, and expectations of those who most depend upon it. Australia's healthcare system should ensure that the consumers (patients) are at the centre of all healthcare decision making and that we measure and monitor the progress of patients. This input extends both specifically from a single treatment or medicine and to the health system more broadly. This will demonstrate real change and overall health and well-being for all Australians.

4. The global context for medicines research, development, manufacture, and supply

The experience of COVID-19 has highlighted how essential global partnerships are in meeting a global health challenge. This has been illustrated through the reliable supply of existing medicines, but also illustrated through global partnerships needed to accelerate the development of diagnostics, treatment options and vaccines.

Medicines research, development, manufacture and supply is conducted globally and will only increase with further globalisation. This means that the market in Australia cannot, and does not, operate in isolation from the rest of the world. Global considerations are frequently applied throughout the medicines systems and processes. This frequency of global considerations is increasing and is particularly evident in specific areas such as global regulatory harmonisation initiatives.

It is imperative that Australia retains its position as a "first wave" country for registration and reimbursement to ensure Australian patients continue to have timely access to innovative medicines and advanced technologies (further detail under TOR 4).

However, as stated earlier, medicines development, manufacture, and supply are conducted globally. Investment faces global competition. Decisions taken elsewhere have consequences in multiple jurisdictions, including Australia, and may occur with little control or influence exerted from Australia. This was exemplified by the recent Executive Order signed by United States President Donald Trump which seeks to lower drug prices in the United States based on referencing the pricing in other countries (see insert below).

Fair pricing in the global context requires that Australia's prices are reasonable in the context of other jurisdictions and the comparative size and impact of the domestic market. Australia should view its prices and pricing policy regime compared to the global context. It is in this context that Medicines Australia member companies consider that Australia does not consistently deliver fair pricing.

One of the consequences of Australia's comparatively low pricing (to rest of world averages) is that Medicines companies in Australia must rely on confidentiality of pricing to ensure that other markets do not either reference or apply Australian-derived pricing to their markets. If confidential pricing is challenged in any way, global parent organisations would likely delay Australia's access to the newest medicines because of the pricing reference risk.

Medicines Australia continues to support the delivery of best value possible. However, modernising and adopting best practice approaches to appropriately valuing medicines, while ensuring greater understanding of the global context, particularly for pricing, will encourage continued investment in Australia's medicines access.

Medicines Australia recommends that there should be a regular forum established to consider global actions and policies that may impact on both Australia's health outcomes and competitive position. This could be the independent oversight committee referred in the recommendations.

US Executive Order

US President Donald Trump has signed the "Most Favored Nation" executive order (EO), which aims to introduce international reference pricing (IRP) into the Medicare pharmaceutical drug programmes (Part B and Part D) to lower drug prices in the United States. The new order calls on the Secretary for Health and Human Services (HHS) to test a new payment model for which Medicare would pay no more than the most-favoured-nation price for "certain high-cost" physician-administered Part B drugs, as well as Part D pharmacy drugs with "insufficient competition". According to the federal administration, the most-favoured-nation price would be calculated as the lowest price for a particular prescription drug or biologic that is sold in another Organisation for Economic Co-operation and Development (OECD) country with a "comparable" per capita GDP to the US.

Most-favoured-nation IRP could lower list prices by up to 80%. An analysis has found that the countries with the lowest prices on average relative to the US were Australia, France, and Norway, despite the latter having a higher per capita GDP than the US in 2018 (OECD; latest available).

Average international-to-US price differential for top 10 Part B and Part D drugs

Country	Australia	Canada	Denmark	France	Germany	Norway	Switzerland
Part B ex-US price differential	-89%	-81%	-84%	-89%	-82%	-88%	-82%
Part D ex-US price differential	-73%	-56%	-65%	-73%	-60%	-72%	-60%
Total Ex-US Price differential	**-81%**	**-70%**	**-74%**	**-81%**	**-71%**	**-80%**	**-71%**

Source: IHS Markit POLI[14]

[14] https://ihsmarkit.com/research-analysis/us-drug-prices-impacted-most-favored-nation-executive-order.html

Conclusion

Medicines are an integral component of healthcare and assist Australians to live longer and healthier lives, remain productive and employed, avoid hospitalisation and positively contribute to the community and the economy. Every innovative medicine made available in Australia has the potential to generate a significant return on investment in the overall health system and economy.

The examples below demonstrate the value of the PBS, and why investment in medicines has such a profound impact on Australia's economy.

Medicines are an investment worth making

- $7 billion was saved in hospital expenditure in 2011 as a direct result of medicines. [15]
- Health strategies for Australians living with osteoarthritis can help recover $1.9 billion in lost super from early retirement and return $3.9 billion to the economy. [16]
- The introduction of new treatments for MS have significantly reduced the economic burden from lost wages over the last 7 years – from 49% to 32%. [17]
- The cost of early retirements due to ill health on GDP was estimated to be $45.3 billion in 2017 and expected to increase to $53.4 billion in 2025. Effective health programs, such as listing of new medicines, can reduce these costs by up to 20%. [18]
- New medicines help reduce the days of hospital care for Australians, helping to reduce hospital expenditure. It is estimated that hospital expenditure in 2015 was reduced by $3.47 billion because of planned investment in medicines in the decade prior. [19]
- The impact of health improvements on gross domestic product has been well documented in a report from the Australian Government's Office of the Chief Scientist. [20] The report noted that if a 10% health improvement were applied to the entire working age population (say, 18 to 69), the expected change in GDP would be around 0.216%, or $2 801 million. The estimated impact of advanced biology on health outcomes was 18% to 34%; this means that the expected change in GDP may be between $5 042 million and $9 523 million.

Australia's PBS has delivered universal access to medicines for Australians for 70 years and continues to do so in a fiscally self-sustaining manner. It has helped to improve the health and well-being of Australians. In return the Government has been repaid with increased productivity and broader economic prosperity, all contributing to the strength and resilience of the Australian economy.

It is Medicines Australia submission that the Government needs to increase the nation's agility and capacity to introduce innovative medicines. The challenge of the COVID-19 pandemic comes at a critical time for the medicines sector and reinforces the opportunity which responding to this Parliamentary Inquiry affords. The Inquiry report and associated recommendations, if implemented, will lay the foundations for once again making Australia a world-leading country for medicines access, as well as research and development including clinical trials.

[15] 2019, Lichtenberg F. *The Impact of Pharmaceutical Innovation on Premature Mortality & Hospitalization in Australia 1998-2018.*

[16] https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2019/08/20160905-rpt-FINAL-Schofield-OA_productivity-final-report.pdf

[17] UTAS and Menzies Institute for Medical Research, Health Economic Impact of Multiple Sclerosis in Australia in 2017

[18] 2018, The McKell Institute, '*Our Health Our Wealth, The Impact of Ill Health on Retirement Savings in Australia',* https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2018/09/Our-Health-Our-Wealth-full-report.pdf.

[19] 2019, Lichtenberg F. *The Impact of Pharmaceutical Innovation on Premature Mortality & Hospitalization in Australia 1998-2018.*

[20] Australian Government Office of the Chief Scientist. The importance of advanced biological sciences to the Australian economy. January 2016. The report noted that if a 10% health improvement were applied to the entire working age population (say, 18 to 69), the expected change in GDP would be around 0.216%, or $2 801 million. ` The estimated impact of advanced biology on health outcomes was 18% to 34%; this means that the expected change in GDP may be between $5 042 million and $9 523 million.

PART 2: RESPONSE TO SPECIFIC TERMS OF REFERENCE

Terms 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 interface between drugs and novel therapies.

Delivering authentic healthcare innovation worldwide that makes a difference in people's overall health status and quality of life is a complex process. This requires a sharp focus on patients' needs, research and development, and availability of pharmaceutical and biotherapeutic products.

The discovery process includes early phases of research where investigational drug therapies are identified and initial testing is conducted in a laboratory setting to determine key determinants of the drug's potential. This includes identification or design of an active component, or serendipitous discovery, and leads to synthesis, screening, assays and exploration of therapeutic value. This first stage of the process takes approximately three to six years. By this stage, researchers hope to have characterised a promising drug candidate for further study in the laboratory, before advancing to testing in animal models, and eventually to trial in people. It takes at least ten, and up to fifteen or more, years for a new medicine to complete the journey from initial discovery to the marketplace, with clinical trials alone taking six to seven years.

We are now in a new era of medicine, where breakthrough science is transforming care and altering the approaches to treating patients. In the last decade alone, biopharmaceutical companies invested half a trillion dollars in R&D. These investments are yielding results, opening the door to entirely new ways to tackle some of the most complex and difficult to treat diseases of our time.

As a result of this tremendous progress, many diseases, previously regarded as deadly, are now manageable and potentially curable. Advancements in science and technology are changing the way we define disease, develop drugs, and prescribe treatments. The promise of personalised medicine (or precision medicine) is to get the right treatment, to the right patient, at the right dose, the first time through the use of molecular diagnostic tests and targeted therapies.

Personalised medicines can potentially offer patients faster diagnoses, fewer side effects and better or more enduring outcomes. At present there are as many as 7,000 distinct types of rare and genetic diseases and 95 per cent of these identified diseases have no approved medicines. A recent American industry survey revealed that 42% of new medicines in the pipeline have the potential to be personalised medicines.[21]

Today, there are more than 8,000 medicines in development around the world. Across the medicines in the pipeline, 74% have the potential to be first-in-class treatments, representing entirely new approaches to treating a disease. The future has never been brighter, as researchers explore new frontiers that just a few years ago may have been regarded as science fiction, but now transform patients' lives.

An example of new drugs and emerging novel medical technologies is the area of cell and gene therapy.

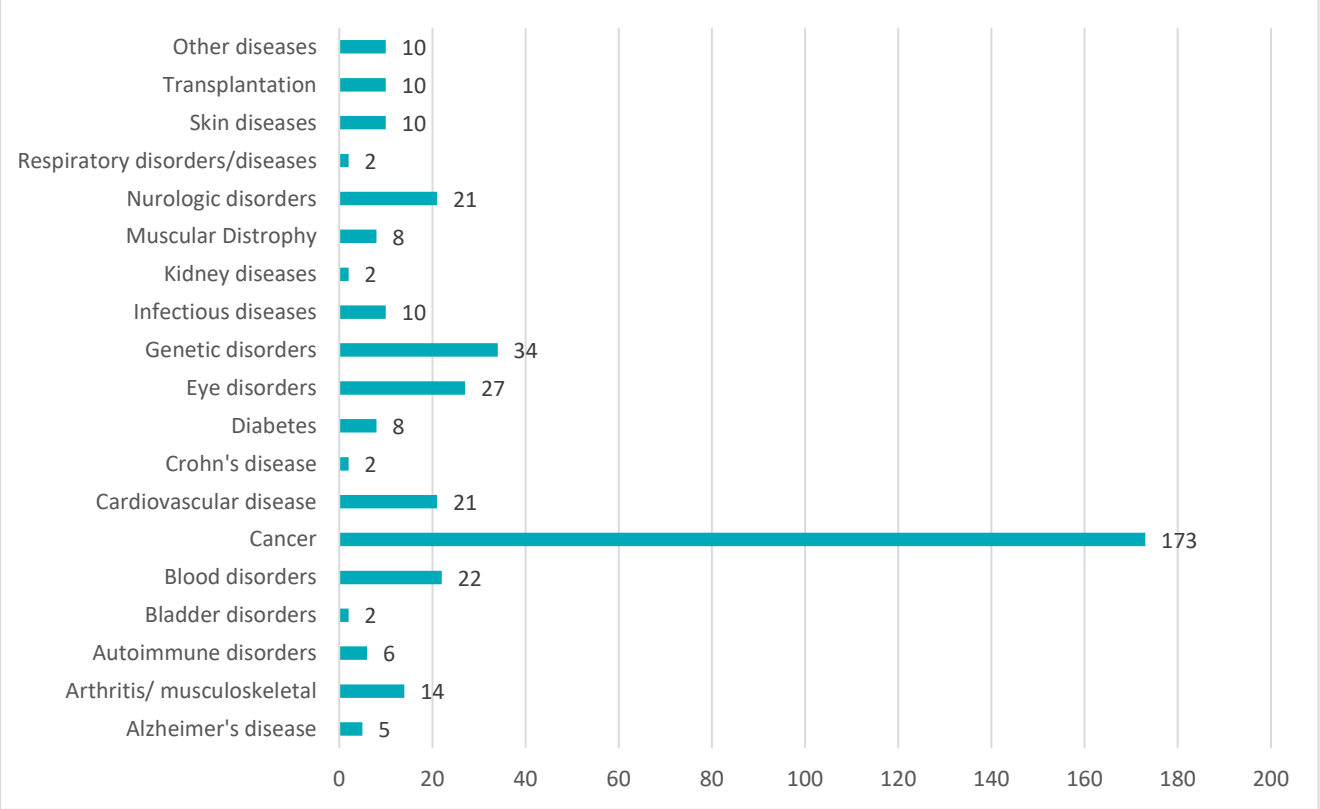
Cell and Gene therapy

Novel cell and gene therapies in the development pipeline today are the result of pioneering research by local and global biopharmaceutical research companies. While there are hundreds of potential cell and gene therapies in the pipeline in the United States, a few of these innovative medicines have already been approved by the U.S. Food and Drug Administration (FDA) and are helping patients today. Currently, data shows there are 362 (Figure 2) novel cell and gene therapies ranging from early to late stages of clinical

[21] https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/rd_brochure.pdf

development in the United States.[22] These are focused on a broad range of diseases and conditions from cancer to genetic disorders to neurologic conditions.

Figure 2: Cell and gene therapy: medicines in development in various disease area (2020)



One third of these cell and gene therapies are in development for rare diseases. As of February 2020, there are nine cell or gene therapy products approved in the U.S. treating cancer, eye diseases and rare hereditary diseases.[23] The FDA has indicated that it expects to approve 10 to 20 new cell and gene therapies between now and 2025.

Cell and gene therapies are fundamentally different from more common medicinal products, as they generally have longer than average development times, more stringent manufacturing requirements, and a limited shelf life for products (sometimes as little as 24 hours).

There are issues facing the regulation of cell and gene therapies in Australia that may be addressed by this review.

For example, the TGA is responsible for assessing quality, safety, and efficacy for market access of therapeutic products. The Review of Medicines and Medical Devices Regulation (MMDR) in 2016 led to the introduction of improved *expedited* regulatory pathways. The resulting TGA *expedited* pathways for registration (*priority review and provisional determination*) are available for prescription medicines, which includes gene therapies. However, such expedited reviews are not available for biologicals, which includes cell and gene-modified cell therapies. The nature of new technologies and the promise they bring lends themselves to attracting a priority status for consideration by the regulator to accelerate patients' access.

Clinical Trials are a fundamental component of the evidence development for all treatments. In Australia clinical trials must be registered with the TGA before they are undertaken. The majority of clinical trials fall under the clinical trial notification scheme (CTN) that enables prompt notification of clinical trials proposed to be undertaken in Australia. However, most cell and gene therapies going into clinical trials in Australia use

[22] some medicines are in more than one category
[23] https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/A-C/MID-cell-and-gene-therapy-2020.pdf

the clinical trial exemption (CTX) route as they are generally classified as biologicals and many are considered class 4 biologicals.[24]

Currently, there is no fixed time for completion of a CTX review (for example, compared to a 30-day turnaround by the FDA on an investigational new drug (IND) application). Further, there is no opportunity to update an application should more information become available while under review.

The classification of biologicals, and drug substance versus drug product when it comes to cell and gene therapies, are not clear across international jurisdictions. The definitions affect the compilation of the Common Technical Document (CTD) for registration of a cell-based therapy.

These issues are further explored under Terms of Reference 4 and a comprehensive outline of medicines in the research pipeline can be found in the Appendices.

[24] https://www.tga.gov.au/book-page/ctn-and-ctx-schemes

Terms 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.

Successful innovation incentives are founded on creating a sustainable and growing ecosystem of domestic and international partnerships for research and development and subsequent commercialisation. This also opens advanced manufacturing and export opportunities. R&D is key. Trusted partnerships are essential.

The COVID-19 pandemic has reinforced that a global problem needs a globally supported solution. One of the Australian pharmaceutical industry's roles during the pandemic has been to contribute to international research and development efforts in developing diagnostics, treatments, and vaccines.

Incentivising an eco-system of partnerships for research and development through to commercialisation in the innovative pharmaceutical industry must be underpinned by a recognition that Australia is part of a growing global network. A network in which Australia can play a leading global and, especially, regional role. As discussed in the subsections below, Australia can better incentivise the pharmaceutical sector through:

- stable, predictable, and focused tax incentives
- strong and reliable Intellectual Property protections
- a more efficient clinical trials environment (see Term of Reference 3: Clinical Trials)
- enhancing commercialisation opportunities
- a better skilled and experienced domestic and migrant workforce

While it is difficult to quantify the value of potential growth in research and development and commercialisation, it is worth highlighting that Australian pharmaceutical company research and development spend of $1.5 billion[25] in 2018 is approximately 0.85% of world total expenditure, which stood at 172 billion,[26] and which may be even higher. This investment has the potential to grow, should Australia's policy approaches be amended to align with global best practice.

For example, if the Australian industry's research and development spend were to grow to 1% of global spending, it would be worth some $2 billion dollars. At 2% of global R&D spend, it would be $4 billion. Australia, and Australian patients, should not miss out on the opportunities that this could bring, especially when the industry is seeking to invest more – under the right conditions.

The alternative is that the R&D happens elsewhere, Australia misses out on jobs, knowledge, and access to the most innovative drugs in the world.

Encouraging Research and Development, including Clinical Trials

The ambition of Medicines Australia's members, alongside the innovative health sector, is to increase research and development in Australia, including between Australian researchers and their international peers. Supporting the ecosystem of research and development partnerships means doing so in Australia and overseas, particularly in a globally supportive pharmaceutical industry.

Medicines Australia has raised concerns where this ambition is hindered by Government policy, including through proposed changes that weaken the value of the Research and Development Tax Incentive (RDTI) scheme, which has generated ongoing investment uncertainty.

[25] https://www.mtpconnect.org.au/images/2019%20MTPConnect%20Sector%20Competitiveness%20Plan.pdf
[26] https://www.evaluate.com/sites/default/files/media/download-files/WP2018.pdf

Medicines Australia has consistently advocated for a research and development environment that facilitates the discovery of innovative pharmaceuticals, vaccines, biotherapeutics, and manufacturing processes, such as through an RDTI scheme that recognises that research and development in the life sciences sector provides public welfare outcomes in addition to high-skilled employment, innovation, and economic growth.

In light of the recent revision to the RDTI, some concerns have been lessened. However, Medicines Australia considers that coherent government policy making will ensure that the impacts of the RDTI are evaluated to ensure that there are no unintended consequences in the life science sector. For example, by regular analysis of the RDTI across the life sciences sector.

Medicines Australia submits that the RDTI should be reviewed to consider:

- Clear and specific exemptions that encourage research and development in life sciences such as benchtop research, clinical trials, and manufacturing.
- Refundable tax offset increase to 45% (an increase of 1.5%) for R&D in the life sciences
- Establishing collaboration premiums for research and development activities, for example, between companies (large, medium, small and start-ups) and publicly funded research institutes through non-refundable tax offsets (e.g. 20%)
- Creating a streamlined and stable system that clearly defines which activities are eligible under the scheme; one that cuts red tape, improves administrative processes, and promotes the integrity of research and development.

Medicines Australia further believes that the Medical Research Future Fund could be realigned to encourage and reward public-private collaboration. For example; Australia could consider using the MRFF to:

- Mirror projects such as the EU Horizon Europe project 2021-2027 (initially intended to provide funding of around €100 billion for research and investment across a range of industries, including medical)[27] to tap into international co-investment and collaboration.
- Promote translational centres of excellence for discoveries of Australian-made products
- Strengthen public-private manufacturing initiatives (such as the CSIRO Innovation fund)

Commercialisation

It has been broadly accepted that Australia needs to enhance collaboration between research and industry to improve translation and commercialisation of research into commercially viable outcomes.[28] Medicines Australia, and many of our members, proudly support *The Bridge Program*, which began in 2017 and selects 100 participants annually from across Australia to take part in face-to-face and online training in the various components that contribute to the commercialisation of new medicines.

A Skilled and Mobile Workforce

Developing, importing, and retaining a skilled, talented, and experienced workforce is vital to research and development, commercialisation, and the growth of the innovative pharmaceutical industry. Our industry employs over 24,600 Australians, many of which are in highly skilled jobs, with above average incomes. As such, Australia's future prosperity will rely on science, technology, engineering, and mathematics (STEM) disciplines that are at the core of innovation.

Yet the industry and the broader health sector in Australia needs access to a more skilled and experienced workforce if it is to capitalise on the growth opportunities. For this, Australia requires a more highly skilled and experienced workforce across the scientific and commercial spectrum; from new graduates to mid-senior scientists, managers, and directors.[29]

[27] https://ec.europa.eu/commission/sites/beta-political/files/budget-may2018-research-innovation_en.pdf
[28] MTPConnect – sector competitiveness plan 2020
https://www.mtpconnect.org.au/images/2020%20MTPConnect%20Sector%20Competitiveness%20Plan.pdf
[29] An industry skills-gap analysis (developed by Medicines Australia, MTP Connect, AusBiotech and ANDHEALTH) is due to be released soon. Medicines Australia will be able to draw upon this report to further elaborate on these issues later in the inquiry process.

For a globalised industry such as ours, our workforce also needs to have international and domestic experience. This can be supported by producing more STEM graduates, continually up-skilling our professionals and through the exchange and utilisation of international talent.

Therefore, Medicines Australia supports investment into STEM education at the primary, senior, and tertiary levels, and professional development programs to produce more experienced graduates and upskill mid to senior level professionals. This is particularly important for girls and women as they are poorly represented in STEM education and the workforce, and women earn less than their male counterparts. [30] Improvement in these areas should deliver the scientific and business leaders that our industry requires to continue growing.

In addition, Medicines Australia encourages the government to develop policies that support international talent exchange that reduce barriers to the unimpeded flow of skilled migration for bringing expertise to Australia. For example, industry requires fast and efficient approvals for long term visas that provide stronger pathways to permanent residency to facilitate faster recruitment of international talent. Such policies will enhance and grow local talent, strengthen our research and development and commercialisation capabilities, whilst also providing opportunities for Australians to work overseas and bring expertise home.

Finally, Medicines Australia would like to see the government work with industry to develop stronger ties between university STEM programs and industry placements to create an environment where industry experience becomes core to the achievement of education. Training and mobility between industry, government and academia will build resilience in the sector and enable the development of truly coherent policy making for job development and sector growth that will support economic recovery.

Strengthening Intellectual Property

Having a strong intellectual property regime is a cornerstone of incentivising not only research and development, but faster commercialisation of pharmaceutical products. This is because companies are more assured, they can get a return on their research and development investment, including for orphan drugs, paediatric uses, and areas of high unmet need. This, in turn, is re-invested in future research and development of new products. If the right intellectual property environment exists, the greater the chance of pharmaceutical discoveries being patented and commercialised in Australia, thereby benefitting Australian patients and Australia's economy.

Regulatory Data Protection (Data Exclusivity)

Whether unilaterally or through international trade agreements, Australia should align its intellectual property regime with key trading partners to boost Australia's competitiveness and strengthen its reputation. The more Australia is aligned with other countries, the more effectively it will compete in the global race for investments in research and commercialisation of innovative medicines. There is an opportunity, including through the current free trade agreement negotiations with the United Kingdom and European Union, to strengthen the intellectual property system to compete with those jurisdictions. In particular, the current system of five years' data exclusivity is less attractive than comparable innovation and investment driven OECD countries (a further explanation of data exclusivity is found at **Attachment 4**).

For example, the European Union provides innovators with ten years of data exclusivity, which can be increased to eleven years for new uses with significant clinical benefit for patients. This comprises eight years data exclusivity, followed by two years "market exclusivity" where a generic company can use the pre-clinical and clinical trial data of the originator in their regulatory applications, but still cannot market their product. This includes for orphan drugs, paediatric uses, and areas of high unmet need (such as for new antimicrobial therapies).

[30] https://www.industry.gov.au/data-and-publications/advancing-women-in-stem-strategy/snapshot-of-disparity-in-stem/women-in-stem-at-a-glance

Patent notification and Market-Sized Damages

Medicines Australia commends the government for recognising the need to resolve longstanding issues relating to the notification of generic and biosimilar medicines entering the Australian market and being listed on the PBS. Recent announcements that will provide greater transparency and timely notification of applications for these medicines to the Australian Register of Therapeutic Goods (ARTG) should pass through Parliament unchallenged. Medicines Australia confirms that improved notification is a condition of the Australia-US Free Trade Agreement and this measure goes some way to resolve the likelihood of potentially unnecessary patent litigation. Other policy measures could also be updated to encourage innovative products in Australia.

For example, to further support these measures, Medicines Australia reaffirms a request to the government to abandon the current policy of seeking damages claims against innovator companies following patent-related legal proceedings. The existing policy creates an unbalanced disincentive to innovator companies to legitimately defend their patent rights. In contrast, in the event that a patent holder successfully defends their intellectual property, there is no mechanism to restore inappropriately applied PBS price reductions instigated by entry of the patent-infringing generic/biosimilar onto the PBS. This, therefore, weights the incentive to generic companies to launch patent infringing products at risk and disincentivises innovators mutual right to uphold and defend legitimate patents. (see **Attachment 4** for detailed explanation of the current context)

These policy approaches create significant uncertainty for pharmaceutical patent holders in Australia and introduces yet another layer of unnecessary litigation. The AUSFTA provides for the creation of a Medicines Working Group that has not met since 2007, but could be reinstated to further explore resolution of this matter.

The importance of this issue was highlighted in the very first recommendation of the Joint Standing Committee on Trade and Investment Growth's[31] recent report:

> *Recommendation 1: The Committee recommends that the Australian Government identify new and emerging trade opportunities and seek to apply the lessons learned from the **Biomedical Translation Fund** to help attract industry investment to those opportunities, as part of an updated trade and investment strategy.*

Whilst we support this recommendation, Medicines Australia submits that more needs to be done across industry, the research and development sector, and government. In particular, the Australian Government (i.e. Department of Health and Department of Industry, Science, Energy and Resources) should work with industry and academia to review how commercialisation can be embedded as part of the research and development culture in Australia. Collaboration will be vital to develop better commercialisation platforms that keep discoveries and their intellectual property in Australia. A culture that values public/private partnerships needs to be fostered, including through government research and development grants, tax incentives and the promotion of venture capital opportunities to fund and commercialise discoveries.

Repurposing older medicines

Incentives, to encourage innovative companies to invest in the level of research required to enable older, legacy products to be repurposed for new uses, are lacking. The costly and uncertain regulatory and reimbursement requirements contribute to this dilemma which ultimately denies patients benefit. The world is struggling to encourage adequate antimicrobial research to combat antimicrobial resistance.[32] Medicines Australia and member companies support initiatives that seek to resolve these issues and encourage new research into new treatments.

There needs to be a framework to rapidly update and/or repurpose older medicines via a simplified regulatory and reimbursement pathway to facilitate improved clinical outcomes for Australian patients.

[31] "Trade transformation: *Supporting Australia's export and investment opportunities"*. The report is the outcome of the Committee's 'Inquiry into Supporting Australia's Exports and Attracting Investment'.

[32] MTPConnect – Australian Antimicrobial Resistance Network. https://www.mtpconnect.org.au/Story?Action=View&Story_id=304

In this regard there is:

- Opportunity to leverage project RENEWAL being undertaken by FDA to update labelling for older cancer medicines should be considered
- Review current barriers to maintaining updated labels based on level of evidence and timelines with the aim of simplifying the framework to enable more timely access for patients
- There are numerous effective therapeutic agents whose side effect profiles have been documented over long-term use in clinical settings that are potential candidates for repurposing. By extending the value and life of the drug by innovative strategies such as reformulation, finding new indications, or rediscovering the inherent value of an old drug, provides added benefit to patients.

Research and development recommendations

Work with industry to review the impact of the revised Research and Development Tax Incentive (RDTI) on pharmaceutical innovation, clinical trials, and innovative manufacturing to identify if further changes are warranted such as:

- Reviewing the need for specific exemptions that further encourage research and development in life sciences; benchtop research, clinical trials, and manufacturing.
- Returning the refundable tax offset to 45% (an increase of 1.5%) for R&D in the life sciences
- Reviewing the need to establish collaboration premiums for research and development activities, for example, between companies (large, medium, small and start-ups) and publicly funded research institutes through non-refundable tax offsets (e.g. 20%)
- Reviewing efficiencies to ensure clarification of which activities are eligible under the scheme; one that cuts red tape, improves administrative processes, and promotes the integrity of research and development.
- Consider potential for the Medical Research Future Fund (MRFF) to be linked or mirrored to the EU's Horizon Europe project.

Terms of Reference 3:

Measures that could make Australia a more attractive location for clinical trials for new drugs and novel medical technologies.

Clinical trials provide measurable health gains to Australian patients, generate new knowledge for a learning healthcare system, and provide spill over benefits to the broader medical research industry and to the Australian economy. Australia currently holds a strong international reputation as a location for high quality clinical trials. Sustaining our success will be a challenge as international competition for the placement of clinical trials has already begun to erode Australia's historical advantages.

In 2019, there were 1,820 ongoing trials in Australia: a 22% increase on 2015. This contributes an estimated $1.1 billion a year to the economy. This figure could easily be doubled over the next 5 years by industry working with governments to create the right settings to realise this ambition. In order to remain a world leader in the delivery of clinical trials, and to attract more clinical trials to Australia, we must be able to:

1. commence trials quickly and in a consistent, harmonised, and efficient manner across multiple centres around Australia
2. Increase the ability for patients to participate in clinical trials. In particular, ensure there is wide recognition and equitable access to clinical trials for patients located in regional areas, through building tele-trials capabilities. This will ensure that clinical trials recruitment is similar to, or greater than that seen in other countries
3. Adopt modern and future-ready technologies to enable clinical trial processes to be conducted efficiently, cost-effectively, and where possible, remotely.

Faster and more efficient start-up of Clinical Trials

The start-up of a clinical trial involves a range of activities, the most significant of which is the ethical review and approval of the trial by a Human Research Ethics Committee (HREC) and the Research Governance review and approval via a Site-Specific Assessment (SSA). These processes are almost always managed consecutively at present, despite local evidence that parallel review significantly increases start-up times[33].

For multi-centre trials conducted across sites residing in different jurisdictions, it is usual to require the services of more than one HREC and each trial site conducts its own Research Governance review. The timelines for review and approval of the trial by both HRECs and Research Governance offices (RGOs) are variable and unpredictable.

The start-up of trials is therefore duplicative, inefficient, costly, and unpredictable in its timeframe, despite reform work that has been undertaken. This is not limited to the start-up of a clinical trial; given both the HREC and RGO will need to continue to be involved in review of certain aspects of the trial throughout its lifecycle this duplication, inefficiency and inflated cost continues throughout the study.

National Harmonisation of Ethics Review

A series of national initiatives intended to contribute to the national harmonisation and streamlining of clinical trial start-up have been implemented at the state, territory, and local level with only limited success. These initiatives include:

- National Mutual Acceptance (NMA) scheme whereby ethical approval of a trial by one Human Research Ethics Committee (HREC) is accepted by others at ***participating public*** hospital centres[34]
- National certification by the National Health Medical Research Council (NHMRC) of ethics committees for multi-centre research[35] [36]

[33] NHMRC, June 2017, Streamlining the site assessment and authorisation of Clinical Trials, Final Report
[34] https://www.australianclinicaltrials.gov.au/ethical-review-process-each-australian-state-and-territory
[35] https://www.nhmrc.gov.au/research-policy/ethics/national-certification-scheme-ethics-review-multi-centre-research
[36] https://www.nhmrc.gov.au/sites/default/files/documents/attachments/list-of-institutions-v42.pdf

- Single point of contact or valet service for trial sponsors[37]

Success has been limited as public health policies do not allow the use of all ethics committees that have been nationally certified by the NHMRC for multi-centre research (e.g. private ethics committees). In addition, public health policies do not routinely allow private research centres to be covered by public hospital ethics committees without a range of varying written agreements in place. As it is very common for a mix of public and private trial centres to be included in trials, at least two ethics committees are required and possibly three if university centres are also involved. This leads to a duplication of effort, increased costs and inefficiency for the initial submission and delays in approval of a clinical trial, resulting in unnecessary delays in patient access to medical treatment.

A National Platform for Ethics and Governance Submissions

The NHMRC developed a portal for the submission of HREC applications. In addition, there are a number of separate and siloed national and state-based portals for HREC and SSA submissions.[38] This creates duplication of information and significant inefficiencies in HREC and Site-Specific Assessment (SSA) submissions. There are significant costs involved across Australia in managing a series of different software platforms that essentially fulfil the same tasks.

Recruitment of Clinical Trial Participants

Australia competes in a regional and global marketplace for participation in the large number of industry-sponsored clinical trials conducted each year across the world. There are a range of factors considered when placing trials in countries including start-up time, cost, and ability to deliver participant recruitment targets[39]. As many as 86% of clinical trials do not reach participant recruitment targets[40] and as such, the ability of sites within a country to recruit to their contracted participant target is a key factor in study placement in the country.

The traditional methods of identifying patients for clinical trials, which take place mostly in large public and private health service organisations, have proven to be adequate at best, but often prove to be insufficient. In order to improve on the ability of investigational sites to recruit to target there needs to be an increase in awareness of the role and importance of clinical trials amongst the general public and the medical community. Clinical trials need to become part of the dialogue between patients and their healthcare providers as a first step towards seeking and identifying appropriate clinical trials. This will be more easily achieved when clinical trials become part of the standard of care in Australia's health infrastructure.

Additional focus on the decentralisation of clinical trials to regional centres, through the utilisation of tele-trials, will provide a broader pool of potential participants by removing the barrier of patients requiring to travel to a metropolitan centre to access a trial. In turn, access to clinical trials becomes more equitable for all Australians, which is especially important given clinical trials can be an important pathway to life saving new treatments.

[37] https://www.svhm.org.au/research/industry/research-valet

[38] For example: HREA.gov.au; REGIS used in New South Wales (regis2.health.nsw.gov.au); ERM used in Victoria & Queensland (au.forms.ethicalreviewmanager.com); RGS used in Western Australia (rgs.health.wa.gov.au); Australian online forms used in South Australia (au.ethicsform.org).

[39] MTP Connect, Clinical Trials in Australia: The economic profile and competitive Advantage of the sector. June 2017

[40] Huang G et al., 2018, Clinical trials recruitment planning: A proposed framework from the Clinical Trials Transformation Initiative. Contemporary Clinical Trials, Vol 66, March 2018, pp74-79

Decentralisation of Clinical Trials

Decentralisation of clinical trials can increase patient diversity in clinical trials, allow faster recruitment to target and ultimately accelerate the development of new treatments. Importantly, it also strengthens the healthcare service in regional areas of the country by exposing doctors and other healthcare professionals to innovations in clinical practice and treatments. Through clinical tele-trials, smaller regional hospitals and clinics can be involved in clinical trials by partnering with larger health service organisations via a hub and spoke model.

Regional participation in clinical tele-trials can also have the effect of ensuring regional centres are firmly included in the learning healthcare system. It would also be an effective way to lift the standard of care and general health care in rural, regional and remote regions – particularly as companies, research institutes in addition to government funding would bring new health, medicines, technologies and supporting infrastructure to areas that would otherwise not receive them. Expanding the areas able to participate in cutting edge research would also attract clinicians to regions where they have previously perceived to be lacking this benefit of a metropolitan centre. Additional clinical trial activity and associated infrastructure requirements may also support jobs.

Modern and Future Ready Technologies and associated practices

The COVID-19 pandemic has seen industry pivot where possible to ensure the continuation of clinical trials that were ongoing during 2020. Trial design, and practices and procedures that had become the norm prior to 2020 for delivering clinical trial design have come under scrutiny. Restrictions on the ability of clinical trial centres to conduct face to face patient visits coupled with sponsor staff being unable to visit centres to conduct monitoring activities, has highlighted the urgent need for technology and accompanying practices to change to allow more efficient and remote ways of conducting clinical trial activities.

While industry can bring new technologies to bear, the healthcare system needs to similarly support clinical trials with remote access to Electronic Medical/Health Records at all clinical trial centres, to accept electronic signatures on clinical trial documentation, to accept e-consent technology[41] and to offer tele-health technologies as routine practice for clinical trial participants (when clinically appropriate). The increased use of these technologies can substantially reduce the workload burden on clinical trials site staff and the healthcare system. The acceptance and support of these technologies and practices are all under scrutiny by global medtech and pharmaceutical companies now and those countries that can undergo rapid adoption will be offered clinical trials preferentially.

41 FDA Guidance Document, December 2016, Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers.(https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-informed-consent-clinical-investigations-questions-and-answers)

Clinical Trial recommendations

1. Update public health policies to provide that the following are mutually accepted by all States, Territories and universities participating in a clinical trial (full detail under TOR 3)
   - *All nationally NHMRC accredited ethics committees can review and approve clinical trials at all public hospitals, private hospitals, trial centres, and universities.*
   - *Approval granted by a nationally NHMRC accredited ethics committee will be mutually accepted by all clinical trial centres without exception and without the need for additional written agreements.*
   - *The Australian Commission on Safety and Quality in Healthcare be tasked to facilitate processes on a national basis to address the items referred to in this recommendation*.

2. Harmonise Human Research Ethics Committee (HREC) and Site-Specific Assessment (SSA) submissions into one Australian online platform; and enable parallel review by HRECs and Research Governance Offices (RGO).[42] The platform should be developed within the purview of the Australian Commission on Safety in Healthcare (ACSQH).

3. Develop and launch a National Community Awareness Campaign for Clinical Trials:
i.e.: NHMRC 'Helping our Health' awareness campaign (or similar) on a sustained or regular basis to boost numbers of patients seeking clinical trials information and that additional national patient awareness campaigns are developed, implemented, and sustained.

4. In consultation with industry, invest in and develop a national standard approach, including nationally agreed systems and standard operating procedures to support and strengthen the capacity to conduct clinical tele-trials in rural, remote, and regional areas, and including regional tele-trials in community awareness campaigns.

5. Invest in and adopt modernised digital technologies and practices to position Australia as the premier destination for international clinical trials (*consult with Industry to develop and introduce national standards for the use of e-consent, e-signature, and electronic medical records to enable remote monitoring and participation in clinical trial across Australia)*

[42] For example, developed under the remit of the Australian Commission on Safety and Quality in Healthcare.

Terms of Reference 4:

Without compromising the assessment of safety, quality, efficacy or cost-effectiveness, whether the approval process for new drugs and novel medical technologies, could be made more efficient, including through greater use of international approval processes, greater alignment of registration and reimbursement processes or post market assessment.

Two key components that enable access to new medicines in Australia are the process for registering a product for marketing in Australia (regulatory); and the process to achieve government subsidy (reimbursement). Both processes are 100% cost-recovered, fee-for service activities provided by the Australian government.

In terms of the regulatory process, the pharmaceutical manufacturer of a new medicine (the sponsor) applies to the Therapeutic Goods Administration (TGA) for registration of a medicine on the Australian Register of Therapeutic goods (ARTG). This is also referred to as market authorisation. The TGA undertakes a thorough assessment of the clinical, non-clinical, manufacturing and quality assay data, collected through years of the medicine's development program to determine its suitability for marketing in Australia. The TGA is considered a Tier 1 regulatory agency and the sovereign capability to reliably determine the quality, safety, and efficacy of medicines for Australians is paramount. Nevertheless, opportunities to improve work-sharing and providing support to the region should be enhanced.

Before any patient in Australia can gain subsidised access to a new medicine, the medicine has to be made available (listed) on the Schedule of Pharmaceutical Benefits through the PBS. This system of determining reimbursement of a new medicine, therapy or vaccine relies on Health Technology Assessment (HTA), a positive recommendation from an appropriate advisory body (such as PBAC or MSAC), and a subsequent bilateral negotiation between the supplier (manufacturer) of the medicine and the monopsony purchaser the Government, represented by the Department of Health.

Of the major submissions considered by the PBAC in 2019, only 39%[43] were recommended following a first submission. The difficulties in navigating through the PBAC and post PBAC processes mean that PBS listings occur later, delaying Australian patients' access to new and innovative medicines.

Table2: Comparison of key metrics for the United Kingdom and Australia HTA Systems

	UK	AUS
% of New Molecular Entity reimbursed 2012-2017	84.3%	46.4%
Avg time from registration to reimbursement	128 days	420 days
% of major submissions recommended after 1st consideration (data from 2019)	90%	39%
Cost per major submission, as of 1 July 2020	$227,027[44]	$335,170[45]

It is imperative for Australian patients that we retain a position as a 'first wave' country for registration and reimbursement to enable early access to innovative medicines and therapies. A system that enables prompt access to innovative medicines in turn supports ongoing R&D investment through early access to new

[43] Based on 2019 PBAC outcome data
[44] Fee for large companies - £126,000 converted to AUD. Fee for small companies - £31,500.
[45] Fee for all companies - includes pre-submission meeting, intent to apply, notice of intent and new deed pricing pathways

therapies and technologies in clinical trials. In contrast, an overly cumbersome regulatory and reimbursement environment adds barriers and disincentives for clinical trials, particularly where the subsequent market entry is uncertain and unpredictable.

The impacts of not being classified as a 'first wave' launch country include:

1. Decreased incentive for global investment in conduct of clinical trials in Australia
    - Reduced options for early access to innovative treatments for patients
2. Delayed regulatory submissions
    - Lack of incentive to use available TGA accelerated pathways (e.g. provisional approvals)
    - Increase use of reliance pathways based on use of overseas evaluation reports reducing TGA global standing as a first-tier regulator undertaking 'de novo' evaluations
    - Delayed access to innovative treatments for Australian patients compared to overseas markets
3. Decision not to file in Australia
    - Reduced options for TGA to gain expertise or workshare with other comparable overseas regulators for 'de novo' evaluations of new innovative medicines and technologies and reducing their standing as a first-tier regulator
    - Differences in standard of care due to available medicine options further reduce attractiveness of Australia for investment in clinical research as per NZ model
    - Impact on generic/biosimilar medicine access pathways due to the absence of comparator innovator registered in Australia
    - Australian patients unable to access latest therapies available in overseas markets

Improving regulatory processes

Following the Review of Medicines and Medical Devices Regulation (MMDR), the TGA introduced new fast track pathways (e.g. priority and provisional registration) to accelerate access to innovative medicines. In parallel it has increased collaboration with overseas regulators through work-sharing opportunities and project ORBIS (see box) to consolidate their position as a first-tier regulator. These initiatives are an important consideration for companies when making decisions on countries to be included in the 'first wave' for regulatory and reimbursement activities.

However, there remain gaps in the availability of accelerated pathways for innovative therapies such as cell therapies and inefficiencies in the workflow of activities across the regulatory and reimbursement processes that can involve multiple bodies. Addressing these issues provides an opportunity for improvements that could speed up access to innovative medicines and new technologies and better benchmark with international best practice.

Project Orbis

Project Orbis is an initiative of the United States Food and Drug Administration (FDA) Oncology Center of Excellence (OCE) and provides a framework where concurrent submission and review of oncology products can be shared between international partners. Collaboration across the FDA, the Australian Therapeutic Goods Administration, and Health Canada may allow patients with cancer to receive earlier access to products in other countries where there can be delays to regulatory submissions.

Table 3: Medicines expedited through Project Orbis[46]

Registration year	Product	Molecule	Therapy area	Number of working days to approval
2019	LENVIMA	LENVATINIB (as MESILATE)	Cancer	54
2019	KEYTRUDA	PEMBROLIZUMAB	Cancer	54
2019	CALQUENCE	ACALABRUTINIB	Cancer	73

Australia-Canada-Singapore-Switzerland Consortium (ACSS)

The Australian TGA is part of the ACSS Consortium, which was formed in 2007 by like-minded regulatory authorities to promote regulatory collaboration[47]. The goal is to maximise the international cooperation and reduce duplication to ensure patients have timely access to therapeutic products.

Table 4: Medicines expedited through ACSS

Registration year	Product	Molecule	Therapy area	Number of working days to approval
2019	VERZENIO	ABEMACICLIB	Cancer	141
2019	ZEJULA	NIRAPARIB (as TOSILATE MONOHYDRATE)	Cancer	180
2020	XOFLUZA	BALOXAVIR MARBOXIL	Other	161
2020	NUBEQA	DAROLUTAMIDE	Cancer	220

Key regulatory issues that impact the timeliness of patient access to new medicines and technologies are outlined below. A summary of procedural improvements that could be implemented to benchmark with international best practice by remodelling regulatory workflows within the existing legislative timelines is presented in the Table below. The full details are at **Attachment 5**.

US and EU		Australia
Clinical Evaluation Resources		
Have sufficient internal resources to undertake clinical evaluations and do not rely on external resources	vs	High level of reliance on external clinical evaluators due to resource constraints.
Evaluation Process		
Single integrated benefit/risk assessment performed	vs	Dual assessment based on initial evaluation reports and subsequent Delegate review of evaluation reports. New issues may be raised late in the process that differ from earlier evaluations.
Multiple rounds of questions allowed	vs	Process is designed based on a single list of questions

[46] Cook,J, 2020. Busting myths about the assessment pathway for new disease treatments for rare diseases. Australian Department of Health.

[47] The Australian Government Department of Health, Australia-Canada-Singapore-Switzerland (ACSS) Consortium, Therapeutic Goods Administration. Note: In October 2020, the United Kingdom regulator, the Medicines and Healthcare Products Regulatory Agency (MHRA), joined the ACSS. https://www.tga.gov.au/acss-consortium-welcomes-uk-its-newest-member

US and EU		Australia
Final evaluation reports represent agency position on data submitted and clearly articulate position on approvability	vs	Uncertainty on approvability due to review of evaluation reports by Delegate which may lead to different recommendations to those in evaluation reports
Advisory/Expert Committee Process		
Transparency of committee proceedings	vs	Sponsors do not receive information on ACM members involved in discussions for their products or the views of members on proposed ACM advice. Other jurisdictions have full transparency.
Sponsor able to present and engage in dialogue with advisory body/committee	vs	ACM meetings are closed to Sponsors whereas Sponsor presentations including support from practicing clinical experts is standard practice in other jurisdictions
Advisory body/committee comprises therapeutically aligned clinical experts and/or regulators	vs	ACM composition include broad range of experts whom may not be experts in therapeutic area

Further, the lack of integration and predictability across the regulatory and reimbursement processes involving multiple bodies extends timelines needed to reach an outcome that enables patient access.

- Uncertainty in predicting regulatory outcomes impacts timing of initiation of reimbursement and limits use of parallel processing that would accelerate patient access
- Regulatory evaluation workflows are inefficient compared to international best practice where a single integrated benefit risk assessment enables Sponsors to predict outcomes and facilitates earlier reimbursement submissions for patient access
- Lack of therapeutically aligned expertise on Advisory Committees and inability for Sponsors to address concerns due to process restrictions can lead to divergent recommendations from other jurisdictions resulting in delays in approval and patient access in Australia
- IT infrastructure is not fit for purpose and impacts efficiency of evaluation workflows including inability to process multiple Clinical Trial Notification (CTN) applications in parallel which delays clinical trial site initiation

Current TGA IT infrastructure has not enabled the TGA to derive metrics requested by industry that would provide meaningful data on performance or implement workflow improvements that would free up evaluation time. The TGA objectives to develop the necessary infrastructure to deliver a fit for purpose regulatory scheme and keep up to date with comparable overseas regulators to support ongoing work-sharing activities is welcomed by industry. In this regard, Medicines Australia welcomes the recent Government commitment to invest $12m over four years to digitise, transform and modernise the TGA's business systems and infrastructure.

Regulatory recommendations:

1. Streamline evaluation process across all independent and government advisory bodies involved in review of new medicines and technologies, where possible
2. Enable a joint Therapeutic Goods Administration (TGA); Pharmaceutical Benefits Advisory Committee (PBAC); Medical Services Advisory Committee (MSAC), Australian Technical Advisory Group on Immunisation (ATAGI) pre-submission advice framework to improve alignment of end-to-end processes.
3. Update TGA regulatory processes to include *expedited* pathways for cell therapies that mirror pathways for prescription medicines, such as *priority review and provisional determination*
4. Introduce statutory 30-day review timeframes and monitoring mechanisms for completion of a CTX review

Improving reimbursement processes

Given the global context for the industry, and for medicines, it is appropriate that the HTA methods and processes employed are equal to, if not better than, internationally recognized best-practice. Industry thrives on global consistency in approach which in turn drives efficiencies. This also ensures that the evidence generation and trial designs are suitable to serve the majority of patient needs globally and reduce the burden of addressing specific outlier requests and methods.

Australia had an advantage with the introduction of Health Technology Assessment (HTA)[48] in 1992 of being among the first in the world to robustly consider cost effectiveness. However, this advantage is now diminished as other markets have caught up and may now be leading change in this area. See **Attachment 3** for examples of reimbursement systems in other countries.

The current HTA system for determining value for money of medicines has not adapted adequately to the changes in the development of medicines and diagnostic technologies, including evidentiary requirements, impacting the access of new and innovative technologies for all Australians:

Full value of medicines needs to be captured

Our HTA system needs to properly value and, therefore, deliver the latest medicines and emerging technologies, applying flexibility and agility to ensure appropriate valuation.

The current PBAC evaluation of medicines, inadequately considers the evaluation of social and economic impacts of a particular medicine or intervention, therefore raising gaps in the assessment process. There are validated methodologies for assessing many of the key determinants of success, used often and with useful context in other areas of health and social research (see Case Study 1 and 3).

In certain areas, the methods used do not appropriately capture the value of the medicine. The resultant impact on pricing is that it may not accurately reflect a treatment's value. Key examples include vaccines and other preventative medicines approaches, where the outcome may be distant to the intervention. There are simple means to address these issues methodologically, even adjusting discount rates in economic modelling; the system ought to be sufficiently flexible to ensure accurate and appropriate valuation.

The issue of appropriate valuation is particularly acute where the value of health benefits and healthcare savings accrue over many years. Future benefits and costs are discounted to reflect society's time preference for benefits now over benefits in the future or the cost of capital. Australia appears to apply one of the highest discount rates in the world to the assessment of future healthcare benefits and costs. [49] (see Case Study 2)

[48] Health Technology Assessment (HTA) is the systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies.
[49] https://www.publish.csiro.au/ah/pdf/AH20057

Case Studies

CASE STUDY 1:

The importance of measuring labour productivity and quality of life as the benefits of interventions for Osteoarthritis:

Osteoarthritis is the most common form of arthritis in Australia. An estimated 2.2 million (9.3%) Australians have this condition, according to the Australian Bureau of Statistics (ABS) 2017–18 National Health Survey (NHS). In 2015–16, osteoarthritis cost the Australian health system an estimated $3.5 billion, representing 28% of disease expenditure on musculoskeletal conditions and 3% of total disease expenditure (AIHW 2019b).

Schofield et al (2016) examined the impacts on economic measures such as personal incomes, welfare payment received and income tax paid associated with productive life years gained of investing in a pharmaceutical intervention using osteoarthritis (OA) as an example in Australia. It was estimated that there would be an additional 1,177 persons in the labour force due to managing their OA with a pharmaceutical product. The estimated cumulative economic benefit of this increased labour participation is $42.7 million per year in annual incomes, an increase of $11.2 million in tax revenue for the Government and a reduction of $15.6 million in welfare payments.

The authors suggested that a well-designed HTA generates highest quality evidence. The authors recommended that economic evaluation of an intervention should be conducted in a societal perspective. A cost-effectiveness analysis of such intervention should be conducted in terms of i) clinical sense (such as improvement in pain score, physical function and need for revision through surgery) and ii) value for money measuring labour force participation (such as productivity gains measuring work capacity), improved quality of life (QoL) (using QoL measure), investigating direct costs (such as healthcare utilization cost) and indirect costs (such as reduced work hours resulting in lost income, reduced tax revenue and dollar value of lost GDP and increased costs of informal care) associated with osteoarthritis (OA) before and after managed by an intervention. The authors indicated that the value of these indirect benefits may be greater than the direct health benefits for certain interventions which was also consistent with previous literature.

CASE STUDY 2:
Discounting of future health benefits in favour of immediate health benefits has devalued health interventions:

A higher discount rate has a large impact on the valuation of interventions with long duration of benefit, for example preventing a death in a young person. Adopting a lower discount rate, in line with international practice (for example, the UK and New Zealand use 3.5% and Canada uses 1.5%), will ensure that long-term benefits and savings associated with preventing or treating long-term diseases are not devalued compared to those countries. For example, Australia places the lowest value on preventing a death in a child with a life-expectancy of 80 years:

Life years saved when preventing a death in a child with a life-expectancy of 80 years:			
Australia	**UK**	**New Zealand**	**Canada**
20.5 life years	27.7 life years	27.7 life years	47 life years

The implications of using relatively high discount rates are that healthcare interventions that reduce risks of ill-health (i.e. preventative health care), such as lipid-lowering drugs, antihypertensives, breast and bowel cancer screening programs and immunisations, will appear less cost-effective and may not be recommended in Australia. Compared with other countries, risk-reducing interventions will appear less cost-effective even if the clinical benefits and costs of delivery are similar.

Where all else is equal, a higher discount rate tips the balance towards approving technologies that yield benefits in the short term. At a time when healthcare systems worldwide are calling for a rebalance of effort towards prevention, Australia's discount rate risks pulling resource allocation in precisely the opposite direction.

Real world data & data collection

For some conditions, real world data (post initial regulatory approvals) may be the only data available. Hence, the methods of evaluation must be made clear so that the industry, consumers, and clinicians may respond with confidence that any research conducted will be of value in decision-making.

An unpublished report for Medicines Australia found that when it is generated using fit-for-purpose data, appropriate methodologies and transparent processes, real world evidence has the potential to reduce uncertainty and enable more informed, evidence-based decision-making across the healthcare ecosystem. The report contends that there are two main challenges associated with generation and provision of real-world evidence as part of the HTA process:

- **Methodological challenges** – where the lack of a specific framework and language for provision of real-world evidence leads to under-generation and under-acceptance.
- **Procedural challenges** – where the pre-reimbursement process is not conducive to the generation of real-world evidence for inclusion in HTA submissions.

In Australia there are further challenges introduced by the comparatively low ability in Australia to link datasets (compared with the rest of the world). This significantly hampers implementation and translational research and makes it more difficult for companies and others making submissions to HTA authorities to address transitivity and applicability issues – particularly if the research has predominantly been conducted overseas.

There is also growing mismatch between consumer expectations for real world data to inform decisions, and its actual use and value in the process. Patient reported outcomes, including non-health outcomes, are tremendously informative for subsequent consumer decision making. The hierarchy of evidence will almost always rely on the highest tier of evidence (randomised trials) but there remains an opportunity to increase patient reported outcomes in trials and linking Patient Reported Outcome Measures to other clinical outcomes. This allows appropriate valuation of the patient reported outcomes in the overall assessment approach.

Improving real-world data collection can assist and improve HTA assessment process and reimbursement decision making. These data provide tangible measurement of effects in the real-world, rather than under the conditions of experimentation required for the unbiased measurement of efficacy.

The efficient adoption of new technologies relies upon continuous improvement of local evaluation and improvement in data collection.

Consistency and alignment across all HTA processes

There remains variability across the HTA assessment processes, not driven by the medicine in question but either by the intended funding mechanism or by the processes used. This has the effect of inconsistencies for industry, and challenges in navigating the process particularly where combinations of modalities or technologies are becoming more common.

Consistency of HTA processes needs to extend from regulatory to the reimbursement process - such as the Pharmaceutical Benefits Advisory Committee (PBAC), Medical Services Advisory Committee (MSAC), and the Australian Technical Advisory Group on Immunisation (ATAGI).

Through years of refining and feedbacks, the Pharmaceutical Benefits Advisory Committee (PBAC) processes are better established, where milestones and deadlines are clearly laid out for companies seeking PBAC consideration of a submission. This is not the case for the Medical Services Advisory Committee (MSAC).

The emergence of co-dependent technologies[50] has highlighted the need for consistent PBAC and MSAC processes to improve efficiencies and ensure patients have access to these technologies. It is common for cancer medicines, particularly targeted medicines, to have an associated diagnostic test or treatment associated device to ensure the medicine is used where most effective. Submissions for targeted medicines partnered with a diagnostic test are complex in terms of content and process. They currently require a separate recommendation from two separate committees with differing meeting schedules- the MSAC for the test and the PBAC for the drug. There appears inadequate interaction between the two committees, and the submission processes vary greatly between the two.

System improvements for co-dependent technologies have failed to address access delays. Drug-test pairings are being penalised by greater complexity and longer timeframes to patient access than pharmaceuticals that do not require an associated test.

As such, it is proposed that there is greater transparency and alignment of the MSAC and PBAC processes and guidelines, including (but not limited to) the publication of MSAC calendar, detailing milestones such as the availability of ratified MSAC Minutes and timing of Public Summary Documents, publication of MSAC agenda and outcomes at specified times (comparable to the long-standing practice of the PBAC).

[50] where the use of a medicine, either sequentially or simultaneously, with the use of diagnostic testing, including genetic testing, to achieve or enhance the intended clinical effect of either technology. MSAC is responsible for recommending diagnostic testings for inclusion on the Medicare Benefits Schedule (MBS).

The uncertain assessment pathways and guidance for new technologies such as gene therapy treatments means that companies are unable to proceed with their submission with confidence, thus increasing submission churn and process inefficiencies. This inconsistency is outlined in the examples below showing the different reimbursement assessment pathway allocated to the same health technologies.

Inconsistencies in the HTA assessment pathways

Luxturna – gene therapy medication for the treatment of Leber congenital amaurosis
Zolgensma - gene therapy medication used to treat spinal muscular atrophy
Kymriah – gene therapy medication for the treatment of acute lymphoblastic leukemia

PBAC	MSAC
• Zolgensma Administered in an hospital (outpatient)	• Kymriah • Luxturna Administered in a hospital (inpatient)

Create additional flexibility and adaptability in assessment and funding for innovation and for new technologies where there are no defined pathways

An emerging issue relates to the lack of flexibility in funding assessment pathways. For some medicines, there appears to be no pathway at all, which acts as a brake on both innovation and access. For others, even as approaching regulatory approval, there is no clarity on the funding pathway.

The current PBAC and MSAC decision-making does not show the same flexibility towards newer technologies when compared with other countries with similar national health systems, for example the UK, Canada, and France. It is argued that the PBAC is often more conservative than its HTA authority counterparts, meaning Australian patients face delays, or miss out entirely on access to new treatments. This is particularly true when considering reimbursement of personalised medicine, preventive medicines, and medicines for small targeted patient populations.

Learning and adopting additional mechanisms from comparable overseas HTA systems can evolve and greatly improve our HTA system's ability to assess newer technologies in a quicker and more flexible manner. As an example, patients in the UK were able to access adjuvant immunotherapy for melanoma 7 days after registration in the UK compared to 177 days in Australia. This was largely due to the UK's Cancer Drugs Fund, which enables early access to innovative treatments while longer-term evidence is being collected. As in the UK example, this flexibility needs to be built around clear and transparent processes backed by independent scientific method.

The PBAC has, in the past, rejected well-established clinical trial design in favour of statistical methodologies that are not internationally accepted. This creates uncertainty for companies with submissions typically relying on well-established and widely used clinical trial designs. Any changes to the assessment criteria need to be done in conjunction with broad public consultation with the scientific community to understand the appropriateness and implications of any new methodology, and to provide certainty to companies.

Improving consumer input to the decision-making process for individual technologies

There has been significant progress in the area of consumer involvement on key decision-making bodies such as the PBAC and others, as well as the inclusion of consumers or community representation on community health boards, ethics review committees and others.

Health technology assessments have increased in complexity making them less accessible for the consumer. Whist those consumers that have access to a group, association, or patient organisation, have a path to develop an aligned and coordinated approach to participation, for consumers with less common conditions, this opportunity may not exist.

With patient participation in HTA being legislated in Germany (2004), Italy (2014) and Taiwan (2016), there is argument for change in legislation to ensure HTA Committees commit to taking account of patient input and patient-based evidence in their documented procedures.

Medicines Australia recommends that all opportunities and mechanisms to contribute to the HTA process should be made consistently available to consumers/patients. A variety of input types/mechanisms to contribute to HTA is important to ensure all individuals with varying levels of resource, capacity, ability, individuals living with disability are taken into consideration during the HTA assessment process.

Medicines Australia also recommends that the HTA assessment process explicitly takes account of social values in addition to clinical cost and effectiveness. This can be done by including consumer engagement throughout its processes. We ask that HTA committees commit to taking account of patient input and patient-based evidence in their documented procedures and terms of reference[51] and include appropriate reporting on this consideration in public summaries. In understanding what is important to consumers, the issues of health impacts are clearly dominant but other factors such as the impact on income generation, social responsibilities and social wellbeing including survivorship are also important. Consumers want to provide more rounded (secondary) impacts of using a medicine, although this is also an area ready for further research and understanding.

[51] Patient Voice Initiative-Summary needs and recommendations August 2018

CASE STUDY 3:
The societal Burden of Haemophilia

Haemophilia is a bleeding disorder caused by a gene mutation which stops blood from clotting properly, causing abnormal bleeding most commonly internal into the joints and/or muscles. There are two types of haemophilia- Haemophilia A or HA (also called classical haemophilia) is the most common type. It is caused by lack of clotting factor VIII, which results from a mutation in gene F8. Haemophilia B or HB (sometimes called Christmas disease) is caused by lack of clotting factor IX, which results from a mutation in gene F9. Some people have mild haemophilia, while others are more severely affected. In the Australian Bleeding Disorders Registry (ABDR), there are currently 2,860 people with haemophilia A and B, with varied degrees of severity. Haemophilia can be complex to manage but it can be managed effectively with appropriate treatment.

Brown et al (2019) conducted a cost of illness study of the potential impact of a pharmaceutical intervention on societal costs based on direct (healthcare utilization costs) and indirect costs (disability pension, informal care and lost wages) associated with HA in Australia. The total treatment related costs including direct and indirect costs of moderate to severe HA were significant, with an estimated cost of over $111 million in 2018, equating to a yearly per patient cost of approximately $120,000. The results of the study indicated that a new pharmaceutical intervention in its first year of use could reduce annual costs associated with moderate/severe HA by nearly $70 million. This reflects a 64% reduction in the cost of FVIII blood products and 92% reduction in cost of bypassing agents. However, the reductions in costs of blood products are expected to be replaced by the cost of the new intervention. The authors also estimated 30.7% reduction in non-treatment direct costs ($3.7 million) and a 19.1% reduction in indirect costs ($2.7 million) including reduced welfare dependence, productivity gains and reduction in need for informal care.

It was concluded that although HA affects only a relatively small number of people within the Australian population, it incurs high aggregate costs and imposes a high economic burden. While treatment costs account for over three-quarters of total costs, the significance of the indirect costs of moderate and severe HA on affected individuals and their families, and on Australian society in general should not be ignored.

This case study demonstrates the significant impact of costs and benefits outside the health system which are inadequately accounted for through the current HTA processes.

Introduce a new oversight committee to provide improved independent oversight of post-PBAC price negotiation process

Since the abolition of the Pharmaceutical Benefits Pricing Authority (PBPA) in 2014, the PBAC has arguably taken a more active role in considering not just the cost-effectiveness of medicines but also budgetary impacts, deeds of agreements, net prices, and risk sharing. Debates have continued about the appropriateness or otherwise of the PBAC undertaking this role.

In Medicines Australia's view, the objectives of the PBAC should be focussed on health technology assessment, and the value for money question. Questions of funding, pricing, business viability and investment should be the remit of a separate body.

The former PBPA had as its objective "to secure a reliable supply of pharmaceutical products at the most reasonable cost to Australian taxpayers and consumers, consistent with maintaining a sustainable pharmaceutical industry in Australia". It provided some semi-independent oversight of the Department of Health's administration of the post-PBAC price negotiation process, where many medicines struggle to achieve PBS listing.

Medicines Australia believes the system would benefit from the introduction of a new oversight committee, which could add value to governmental processes, improve decision making and accountability, and assist in achieving the appropriate balance between value-for-money reimbursement and ensuring sustainable supply.

The structure, objectives, operations and outcomes of the new committee could be determined in dialogue between industry, government and other stakeholders considered appropriate. Such a forum could also consider the global context in which the industry operates.

Re-introduce dialogue between industry and the PBAC to consider future policy issues to guide the HTA process

In the past, there was regular dialogue between Medicines Australia and the PBAC on issues of importance to the HTA process. Medicines Australia believes the re-introduction of such a dialogue would be beneficial, given the lack of certainty for new therapies in terms of HTA assessment. Additionally, it is Medicines Australia's view that the HTA process would benefit from a series of principles to inform the decision-making process. These principles could include such areas as:

- Sound Process: HTA should have a sound process that is open and transparent, with opportunity for input and a strong role for patients and physicians.
- Patient-centred Focus: HTA should be patient-centred and consider individual patient needs and varying responses to treatments.
- Reliable and Relevant Information: HTA should deliver reliable, relevant information using rigorous methods that rely on the full range of evidence and prioritize longer-term and broader outcomes.
- Recognition of Progress and Innovation: HTA should value continued scientific and medical progress and account for the promise of personalized medicine, the stepwise nature of progress and the inherent value of innovation.
- System-wide Perspective: HTA should take a system-wide perspective on value by examining the full range of tests, treatments, care management approaches and health care services

These principles could be the subject of discussion between Medicines Australia and the PBAC.

Reimbursement recommendations:

1. Modernise and improve HTA evaluation processes in line with international best practice HTA and better capture the impact of the social and economic contribution of medicines, such as patient reported outcomes, productivity and community
2. Ensure consistency and alignment across all HTA processes
3. Work with industry to establish and introduce flexible and adaptable assessment models and funding mechanisms which recognise innovation and for new technologies where there are no current agreed/defined pathways.
4. Enable consumers, patients, and patient groups to provide timely and relevant input to the decision-making process for individual technologies through patient led initiatives.
5. Establish a new oversight committee to provide independent supervision of the post-PBAC price negotiation process between industry and government and ensure appropriate risk sharing is put in place.
6. Reinstate annual dialogue between industry (represented by Medicines Australia) and the PBAC to consider and create opportunities to resolve issues of relevance for a contemporary HTA process.

APPENDICES

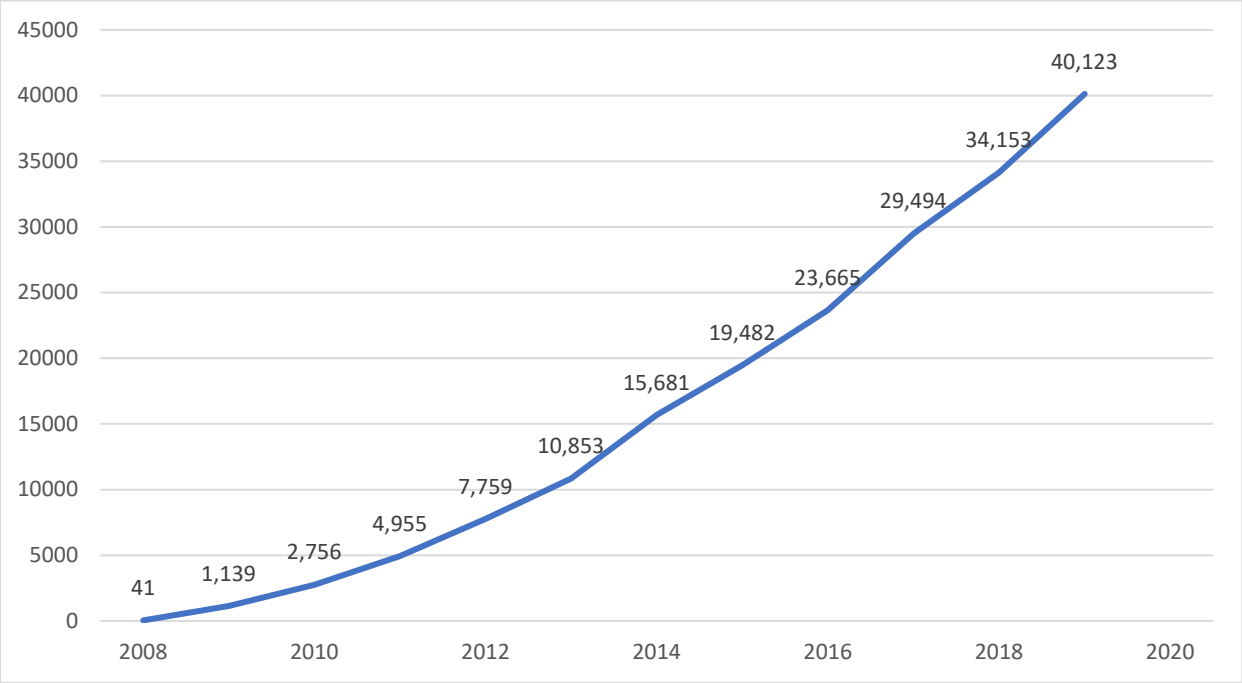
Attachment 1: Pharmaceutical sector: drugs in the research pipeline

Cell and Gene therapy

Cell and gene therapies is an emerging field that offers massive potential to revolutionise treatment of many diseases, particularly cancers, with many clinical trials in progress or having been completed in Australia.

Figure 3 illustrates the number of registered studies conducted in the last decade globally, which reflects the growing investment in researching and developing these therapies.[52]

Figure 3: Number of registered studies (as of November 2019)



These emerging therapies have caught the eye of venture capitalists, who invested more than $16 billion in global biotech during 2019 alone.[53] While there are hundreds of potential cell and gene therapies in the pipeline in the United States, a few of these innovative medicines have already been approved by the U.S. Food and Drug Administration (FDA) and are helping patients today. Currently, there are 362 (see Figure:2) novel cell and gene therapies from early to late stages of clinical development in the United States and are focused on a broad range of diseases and conditions from cancer to genetic disorders to neurologic conditions. [54] One third of these cell and gene therapies are in development for rare diseases. [55] The FDA has indicated that it expects to approve 10 to 20 new C&GTs between now and 2025.

Among the cell and gene therapies in development *(see Figure 2)* are potential treatments for:

- A gene therapy using adeno-associated virus (AAV)-factor VIII is designed to stimulate the production of factor VIII for the treatment of hemophilia A. A gene therapy using AAV vectors is delivering a high-activity Factor IX gene to the liver for the treatment of hemophilia B. Currently in Australia there are 2,800 people with haemophilia A and B, with varied degrees of severity.[56]

[52] https://resources.oxfordeconomics.com/hubfs/Making_cells_better_Complex_challenges_drive_innovation_in_cell_and_gene_therapy_manufacturing_2020.pdf
[53] https://www.svb.com/globalassets/library/managedassets/pdfs/4q_2019_pitchbook_nvca_venture_monitor.pdf
[54] https://www.phrma.org/Science/In-The-Pipeline/Medicines-in-Development; some medicines are in more than one category
[55] https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/A-C/MID-cell-and-gene-therapy-2020.pdf
[56] https://www.haemophilia.org.au/about-bleeding-disorders/fast-facts#splash-timed

- A second-generation CAR-T cell therapy comprised of genetically-modified T-cells, is designed to target B-cell maturation antigen and to redirect the T-cells to recognize and kill malignant myeloma cells.
- A gene therapy for the treatment of Stargardt disease (a genetic eye condition) delivers a corrected version of the ABCR gene directly in the photoreceptors in the retina. There are approximately 2,500 – 3,000 affected individuals in Australia.[57]
- A gene therapy uses a recombinant AAV9 capsid to deliver a shortened version of human dystrophin to treat Duchenne muscular dystrophy (DMD). It is estimated that there are more than 20,000 people in Australia who have some form of neuromuscular disease.[58] Duchenne muscular dystrophy is the most common type affecting children, it affects about one in 3,500 boys. Girls do not usually develop DMD.[59]

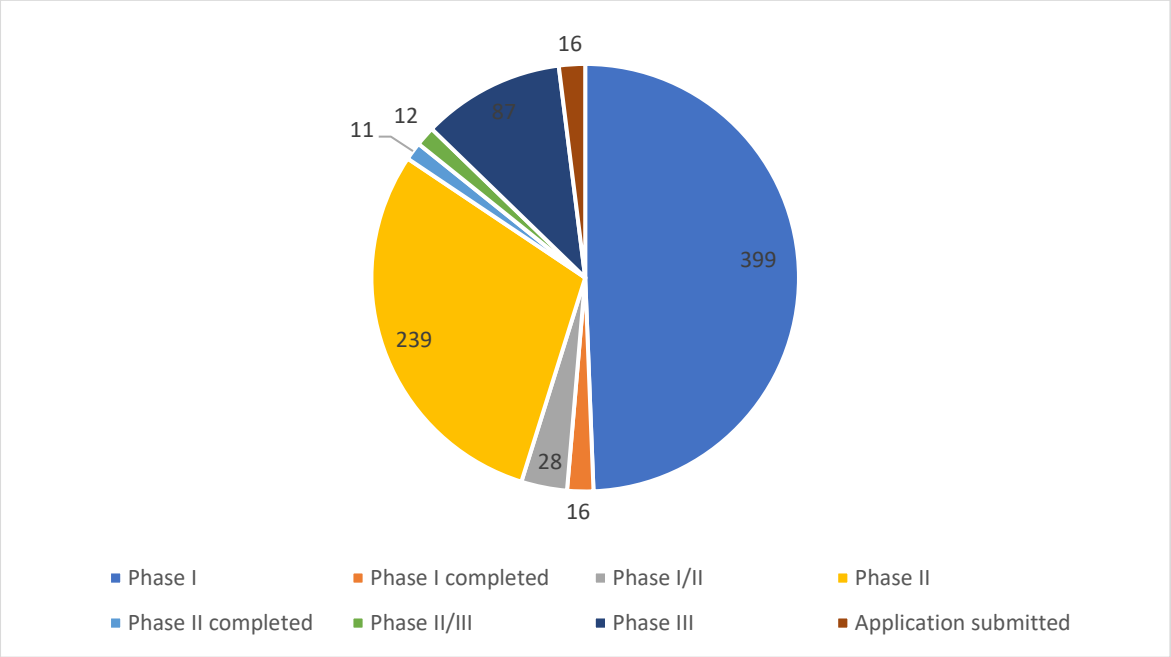
These cell and gene therapies are revolutionising medicine, but scientists and manufacturers still face technical and logistical challenges to bring these treatments to market in sufficient commercial quantities. A recent publication (2020) by Oxford Economics explored these challenges and suggested that large capital investments are likely needed to bring future breakthroughs that will standardize processes, simplify delivery logistics, boost efficiency and increase competition.[60] As researchers explore next-generation therapies, similar innovation needs to occur in the regulatory and reimbursement processes in Australia.

Infectious disease

Although the burden of infectious diseases in Australia is relatively small (2.0% of total burden) (AIHW 2019), most people will experience an infection from a communicable disease during their lifetime—for example, a common cold or a stomach bug. [61] Many infectious diseases have the potential to cause significant illness and outbreaks such as, COVID-19.

A recent report shows more than 400 medicines and vaccines in development to tackle infectious diseases, including COVID-19.[62] Figure 4 shows various phases of medicines in pipeline for treating infectious disease in the US in 2020 [63]:

Figure 4: Infectious Disease: Medicines in Development (2020)

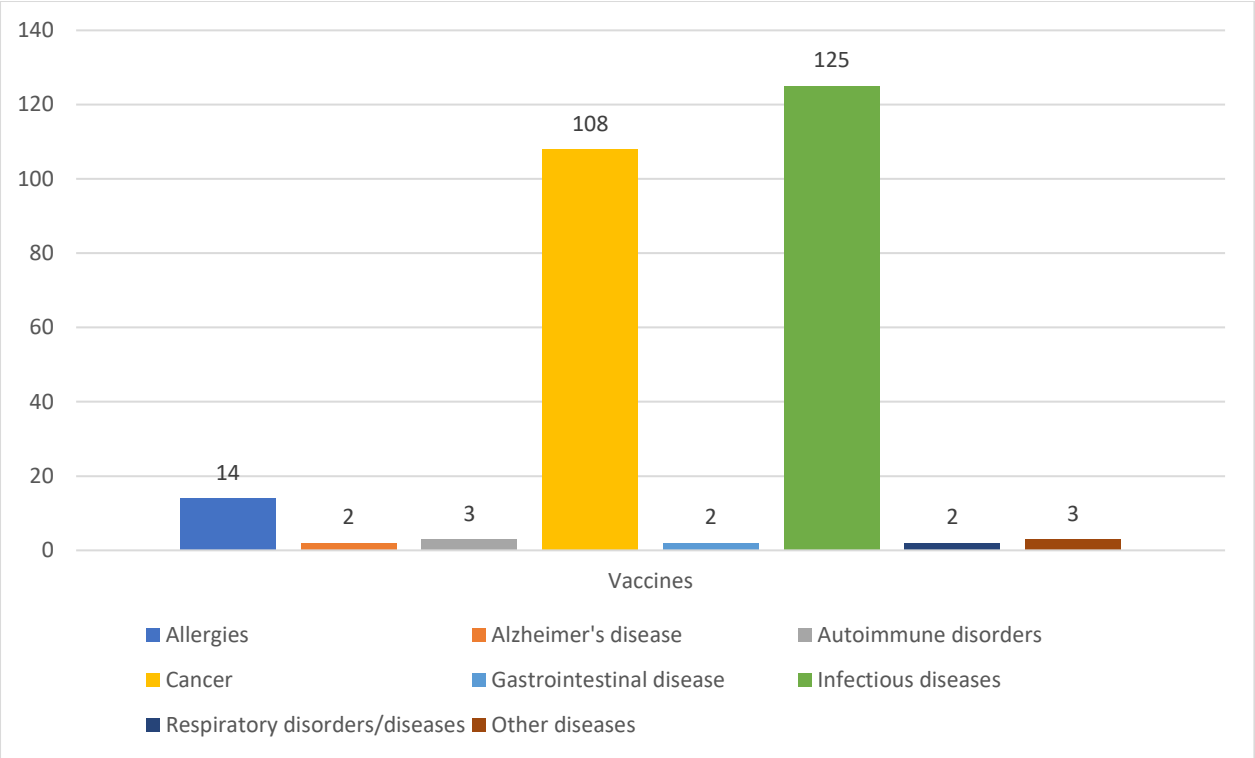


[57] https://www.retinaaustralia.com.au/
[58] https://mdaustralia.org.au/
[59] The Royal Children's Hospital Melbourne, Duchenne muscular dystrophy
[60] Oxford Economics, Making cells
[61] https://www.aihw.gov.au/reports/australias-health/infectious-and-communicable-diseases
[62] https://www.phrma.org/Science/In-The-Pipeline/Medicines-in-Development; some medicines are in more than one category
[63] https://www.phrma.org/Science/In-The-Pipeline/Medicines-in-Development; some medicines are in more than one category

Vaccines in Pipeline

The 258 vaccines in development by biopharmaceutical research companies are being investigated to treat or prevent infectious diseases, cancers, allergies and Alzheimer's disease in the US (see Figure: 5)[64]

Figure 5: Vaccines in pipeline (2020)



Among the vaccines in development are:

- A vaccine to prevent HIV infection, which has the potential to teach the patient's immune system to recognize and effectively fight HIV. This vaccine contains mosaic immunogens – molecules designed to induce an immune response against the wide variety of HIV strains responsible for the epidemic. It is currently being tested for efficacy in large-scale clinical trials taking place across four continents.
- A therapeutic vaccine for non-small cell lung cancer (NSCLC) which uses messenger RNA (mRNA) to mobilise the patient's own immune system to fight the tumor(s). mRNA are the instructions to cells that make all proteins and send them to various parts of the body. mRNA medicines take advantage of the body's biological processes to create a desired therapeutic effect. The vaccine in development targets six specific tumor-associated antigens (substances produced in tumors that trigger an immune response) that are overexpressed in lung cancer (studied in combination with cancer immunotherapy)
- A therapeutic vaccine for Alzheimer's disease targets amyloid beta protein and is designed to induce high B-cell specific responses while avoiding T-cell inflammation, an autoimmune response that can lead to organ damage. In animal studies, the vaccine was shown to generate site-specific antibodies and to reduce amyloid beta.
- An adenoviral vector vaccine for the prevention of respiratory syncytial virus (RSV) infections in adults over the age of 60 contains gene coding for the fusion protein of the RSV virus as an antigen to induce an immune response in the body, especially the production of antibodies.
- A vaccine for the prevention of novel coronavirus (COVID-19) recently dosed the first participant in a clinical trial. The messenger RNA-based vaccine is designed to direct the body's cells to produce proteins (intracellular, membrane or secreted proteins) that can have a preventative benefit against the virus.

[64] Ibid; some medicines are in more than one category

While there are no approved vaccines against COVID-19, there are more than 70 vaccines in the worldwide research pipeline. Six vaccines have entered human clinical trials, while several more vaccines are in preclinical development with many planning to begin human trials this year.

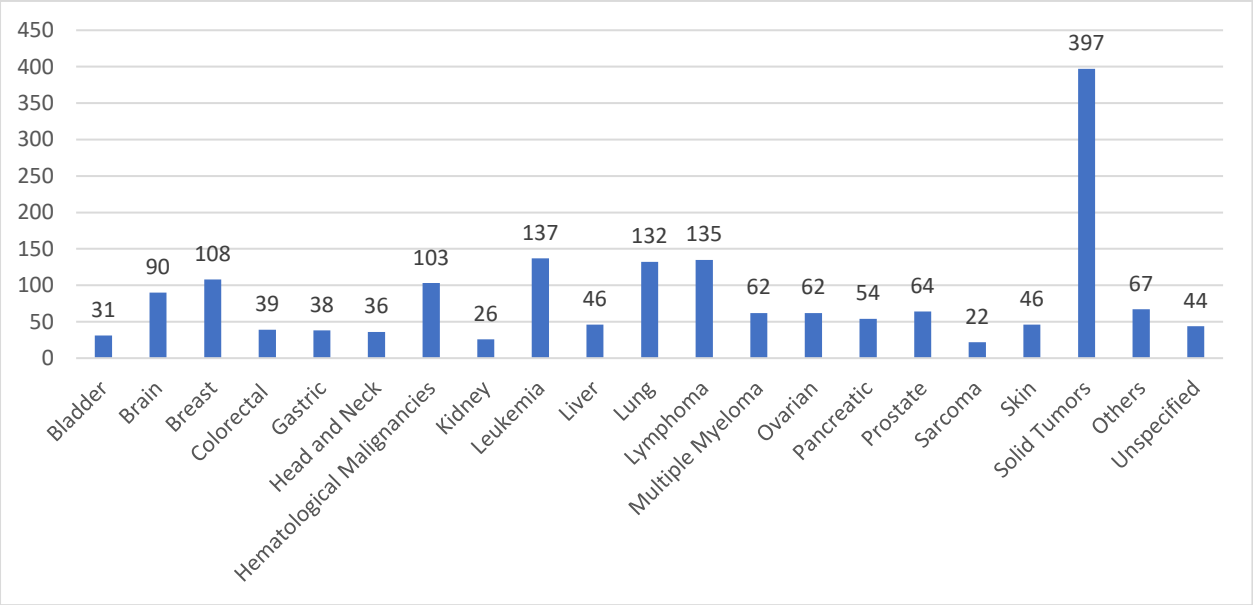
Cancer medicines in pipeline 2018

The impact of cancer on the global community can now be defined with greater precision than ever before. Population-based cancer registries operate in many countries, and data from hospitals and other sources provide a clear indication of cancer incidence and mortality in most other countries. Between 1988 and 2000, treatment advances in cancer have saved 23 million years of life and added $1.9 trillion to society based on improved productivity, extended life and other factors. [65]

Cancer is a major cause of death in Australia and has a substantial social and economic impact on individuals, families and the community. There are over 1 million people alive in Australia who are either living with or have lived with cancer.[66] A study by Bates et al (2018) indicated that 50,100 Australian adults of working age (25–64 years) with cancer were not in the labour force in 2015, thereby reducing Australia's GDP by approximately $1.7 billion.[67]

More than 1,100 cancer treatments in clinical testing offered hope to patients as of 2018 in the US (see Figure 6).[68] An average of 85 percent of medicines in the oncology pipeline were likely to be first-in-class medicines, meaning they used a new and unique mechanism for treating a disease.[69]

Figure 6: Medicines in development for Cancer (as of 2018)



[65] http://phrma-docs.phrma.org/files/dmfile/2018_MID_Cancer.pdf
[66] https://www.aihw.gov.au/reports/cancer/cancer-in-australia-2019/contents/summary
[67] https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-018-5297-9
[68] https://www.phrma.org/Report/Medicines-in-Development-for-Cancer-2018-Report; some medicines are in more than one category
[69] 2018 Cancer Chart Pack, PhRMA

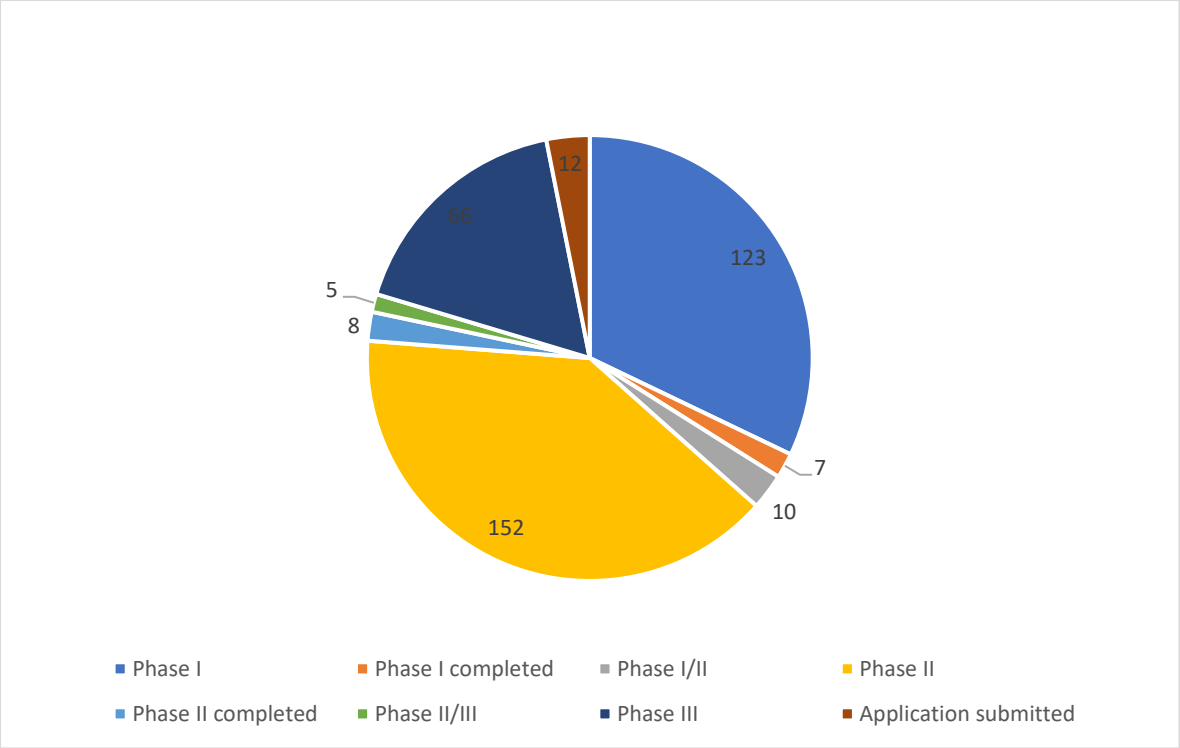
Australia's most deadly diseases other than cancer and their medicines in pipeline

Coronary heart disease, cerebrovascular disease including stroke, dementia including Alzheimer's disease are the leading burden of diseases causing death in Australia.[70]

An estimated 1.2 million (5.6%) Australian adults aged 18 years and over had 1 or more conditions related to heart or vascular disease, including stroke, in 2017–18, based on self-reported data from the Australian Bureau of Statistics (ABS) 2017–18 National Health Survey. [71] And there were around 583,900 hospitalisations with cardio vascular disease as the principal diagnosis (the diagnosis largely responsible for hospitalisation)[72] creating a significant burden on the healthcare system.

Figure 7 shows various phases of medicines in pipeline to treat Heart disease and stroke in the US:[73]

Figure 7: Heart disease and stroke: Medicines in development (as of 2018)

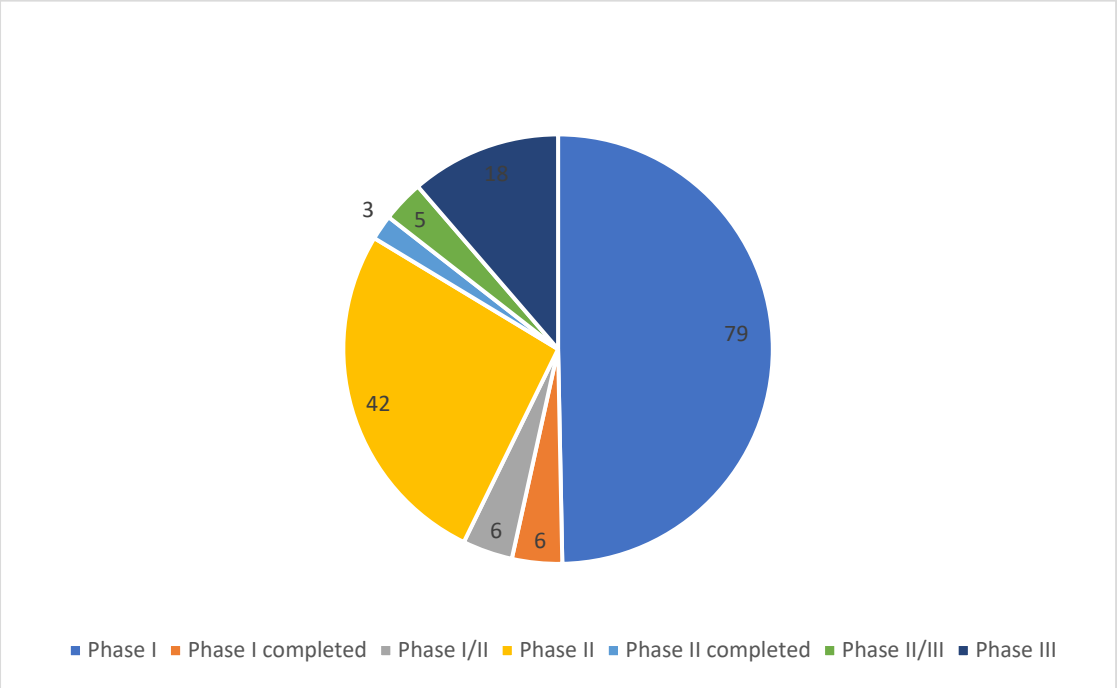


Alzheimer's disease affects millions of patients worldwide and costs billions of dollars annually. It is estimated that in 2020 there are between 400,000 and 459,000 Australians with dementia (AIHW 2018; DA 2020), with Alzheimer's disease accounting for up to 70% of diagnosed cases (DA 2018). By 2025, the total cost of the disease is predicted to increase to $18.7 billion in today's dollars and by 2056, to more than $36.8 billion.[74]

Figure 8 shows various phases of the pipeline of drugs in clinicals trials for the treatment of Alzheimer's disease in the US. [75]

[70] https://www.aihw.gov.au/about-our-data/our-data-collections/national-mortality-database; https://www.abs.gov.au/ausstats/abs%40.nsf/mf/3303.0/
[71] https://www.aihw.gov.au/reports/heart-stroke-vascular-disease/cardiovascular-health-compendium/contents/how-many-australians-have-cardiovascular-disease
https://www.abs.gov.au/statistics/health/health-conditions-and-risks/national-health-survey-first-results/latest-release
[72] https://www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium/contents/hospital-care-for-cardiovascular-disease
[73] https://www.phrma.org/en/Report/The-Biopharmaceutical-Pipeline; some medicines are in more than one category
[74] https://www.dementia.org.au/dementia-news/issue-07/economic-cost-of-dementia
[75] https://www.phrma.org/en/Report/The-Biopharmaceutical-Pipeline; some medicines are in more than one category

Figure 8: Alzheimer's Disease: Medicines in Development (as of 2017)



Diabetes medicines in pipeline (2019)

Diabetes is recognised as the world's fastest growing chronic condition. In 2019. Approximately 463 million adults (20-79 years) were living with diabetes. [76]An estimated 1.2 million Australians (4.9% of the total population) had diabetes in 2017–18.[77] A recent study by Schofield et al (2017) [78] was conducted on the societal costs of diabetes among Australians aged 45–64 years from 2015 to 2030. The study indicated that 18,100 people were out of the labour force due to diabetes in 2015, increasing to 21,400 in 2030 (18% increase). National costs consisted of a loss of $467 million in annual income in 2015, increasing to $807 million in 2030 (73% increase). For the government, extra annual welfare payments increased from $311 million in 2015 to $350 million in 2030 (13% increase); and lost annual taxation revenue increased from $102 million in 2015 to $166 million in 2030 (63% increase).

Figure 9 shows number of medicines in pipeline for the management of diabetes and related comorbidities in the US in 2019: [79]

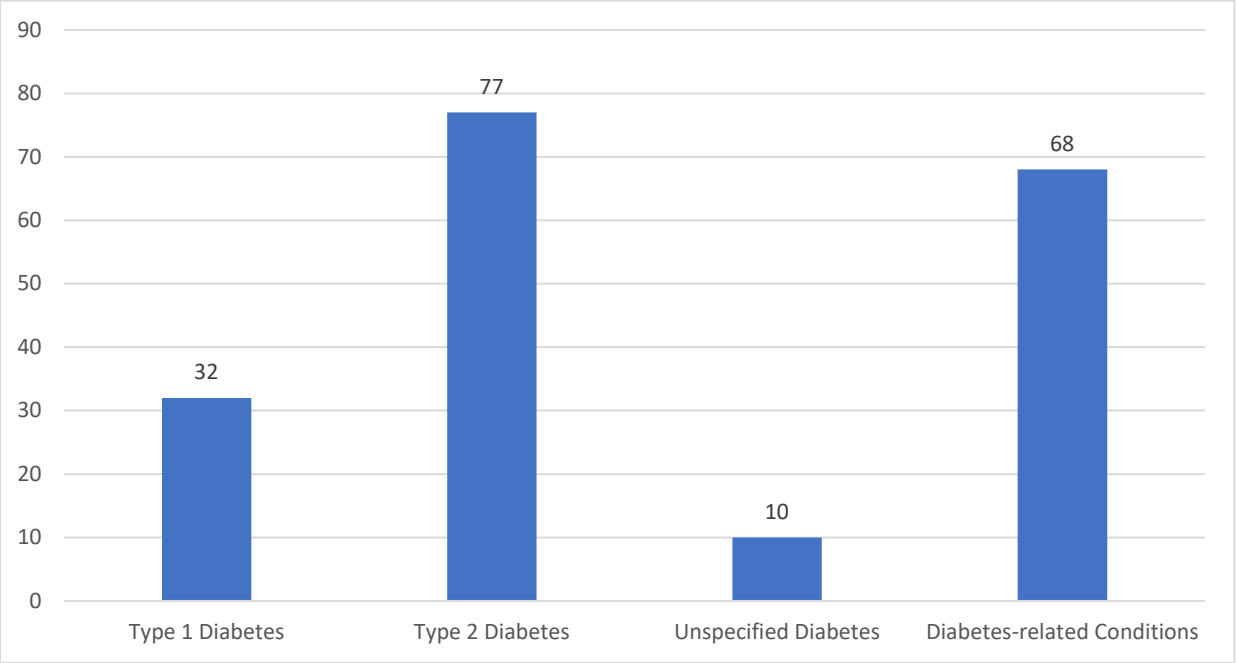
[76] https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html

[77] https://www.aihw.gov.au/reports/diabetes/diabetes/contents/how-many-australians-have-diabetes

[78] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5223630/

[79] https://www.phrma.org/en/Report/The-Biopharmaceutical-Pipeline; some medicines are in more than one category

Figure 9: Diabetes; Number of medicines in development (as of 2019)



The 167 innovative medicines in development for type 1 and type 2 diabetes and related conditions include:

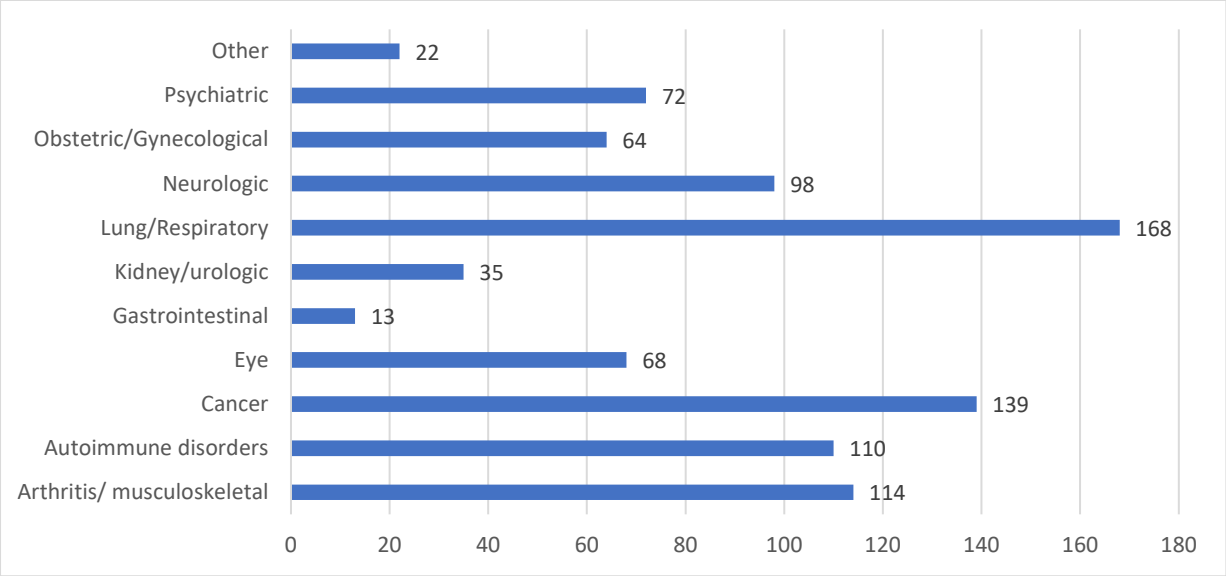
- **77 medicines for type 2 diabetes**: In type 2 diabetes, which comprises up to 95 percent of diagnosed diabetes cases, the body is resistant to the action of insulin. To combat this resistance, the pancreas makes even more insulin until it fails to produce enough insulin to overcome the resistance, causing blood glucose levels to be higher than normal.
- **32 medicines for type 1 diabetes**: Type 1 diabetes, which comprises about 5 percent of diagnosed diabetes cases, is an autoimmune disease where the body does not produce insulin as a result of the immune system attacking the insulin-producing cells of the pancreas. It is usually diagnosed in children and young adults and requires lifelong insulin treatment for survival.
- **68 medicines for diabetes-related conditions**: These include chronic kidney disease due to diabetes (diabetic nephropathy), painful diabetic neuropathy, diabetic macular oedema, and diabetic gastroparesis.

Women's and paediatric drugs in pipeline

The health of our nation depends on the combined and individual health of Australians. Healthier women and their children contribute to more productive and better-educated societies. Recognising that women's experiences of mental and physical illness are different from men's is essential for developing treatment options that are effective in addressing the health needs of women and girls in Australia.

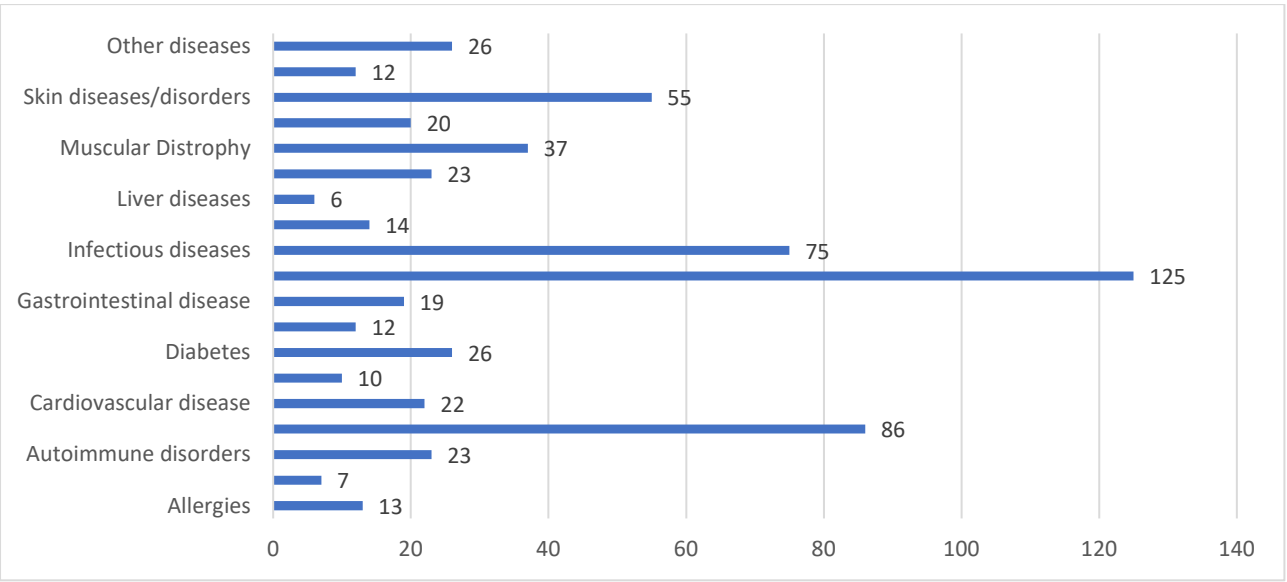
In 2013, 851 medicines were being developed for diseases that disproportionately affect women in the US.[80]

Figure 10: Medicines in development for women (as of 2013)



The health of children and young people is fundamental to the ongoing prosperity and cohesion of Australian society. A robust drug development pipeline offers tremendous promise for the future. Currently there are over 2,100 industry-sponsored paediatric clinical trials underway (see Figure 11 for number of medicines in pipeline for paediatric patients in the US)[81], across a variety of therapeutic areas, including diseases where there is significant unmet need, such infectious diseases, neurologic conditions, genetic disorders, and several forms of cancer.

Figure 11: Paediatric medicines in development (2020)



[80] https://www.phrma.org/Science/In-The-Pipeline/Medicines-in-Development;some medicines are in more than one category

[81] Ibid; some medicines are in more than one category

The innovative biopharmaceutical industry is firmly committed to conducting paediatric research and is making great strides against paediatric illnesses. Recent research has provided important new dosing, safety and efficacy information in paediatric populations that is changing the treatment landscape across a range of serious and life-threatening diseases, including:

- **Asthma**: Paediatric patients age 6 to 11 now have a therapy option that addresses severe eosinophilic asthma, a complex and challenging condition to treat, which was previously only approved for use in children age 12 and older. This breakthrough is a significant step forward, as asthma is the third-ranking cause of hospitalization among children younger than 15. In 2017–18, an estimated 10% (around 460,000) of Australian children aged 0–14 were reported to have asthma as a long-term condition. Asthma prevalence was twice as high among children with disability (18%) compared with children with no reported disability (8.9%). [82]
- **Type 2 Diabetes**: The first non-insulin drug approved to treat type 2 diabetes in paediatric patients is now available. The medicine enhances the incretin system, a natural body system that helps to regulate glucose, and improves blood sugar control. Australian research suggests that the diagnosis rate of type 2 diabetes in children is increasing, likely due to the increase of childhood obesity (NDSS 2019).[83]
- **Peanut Allergy**: A new oral immunotherapy designed to reduce the incidence and severity of allergic reactions due to accidental peanut exposure is now available for children with peanut allergy. The therapy delivers a controlled daily dose of peanut protein that is gradually increased over months to build tolerance in the immune system's overreaction to peanuts. Almost 3 in every 100 children have a peanut allergy.[84]
- **Rare Genetic Brain Tumour**: Children with a rare genetic disorder, tuberous sclerosis complex (TSC), now have a treatment option for tumours that occur in the brain. This new development offers a dissolvable dosage form that is easier to take for paediatric patients. TSC affects more than 2,000 individuals including kids in Australia and thousands more carers, families and friends who live with the impact of the disease. [85]
- **Chronic Myelogeneous Leukemia**: Additional research revealed that a breakthrough targeted therapy for this rare blood cancer is safe and effective in very young children, offering an important treatment option for physicians to use in treating this rare blood cancer. In 2017, Leukemia was one of the leading causes of Cancer in children in Australia.[86]

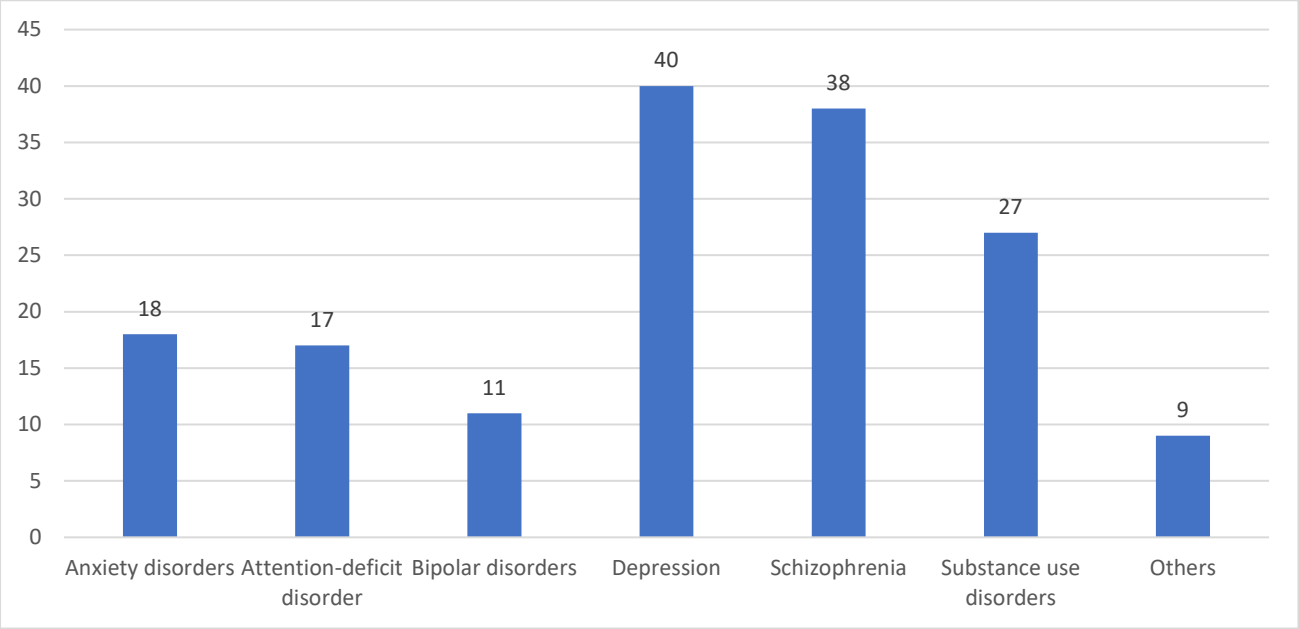
[82] https://www.aihw.gov.au/reports/children-youth/australias-children/contents/health/asthma-prevalence-among-children
[83] https://www.aihw.gov.au/reports/children-youth/australias-children/contents/health/children-diabetes
[84] https://allergyfacts.org.au/allergy-anaphylaxis/food-allergens/peanut
[85] https://tsa.org.au/
[86] https://www.aihw.gov.au/reports/children-youth/australias-children/contents/health/cancer-incidence-and-survival

Mental illness drugs in pipeline 2019

Mental illness takes a heavy personal toll on the patients, caregivers and loved ones who are impacted. One quarter of Australians aged 16 to 85 years (4.2 million people) will experience an anxiety condition during their lifetime. Women are more likely than men to experience depression and anxiety. [87]Almost 14 per cent of young people aged 4 to 17 years (or 560,000 people) experienced a mental disorder in the 12 months between June 2013 and April 2014. The cost of mental ill-health in Australia each year was around $4,000 per person, or $60 billion in total and mental ill-health in the workplace costs an average of $3,200 per employee with mental illness, and up to $5,600 for employees with severe mental illness. Overall, it was estimated that the cost of workplace mental ill-health in Australia was $12.8 billion in 2015–16.[88]

The development of new and effective treatments for mental illness is very difficult, given the scientific complexities underlying the cause of many of these diseases. Despite these challenges, biopharmaceutical research companies had 138 medicines in development in the US as of 2019 (see Figure 12) which offer a promise to help the millions of people living with mental illness.[89]

Figure 12: Mental illness: Number of medicines in development (as of 2019)



The medicines in development include:

- **40** for **depression**, including major depressive disorder which affects 1 million adults in Australia each year. [90] Approximately one-third of adults with major depression have treatment resistant depression where currently available treatments provide little to no relief, representing a significant unmet need.[91]
- **38** for **schizophrenia**, which affects every 1 in 100 Australians and approximately 20 million people worldwide (Healthdirect 2018, WHO 2019).[92] Schizophrenia is a chronic and severe mental disorder that affects how a person thinks, feels, and behaves. This disease in particular is especially debilitating as it can result in psychotic behaviours like hallucinations and other disruptions to normal emotions and behaviours.

[87] https://www.health.gov.au/health-topics/mental-health#:~:text=One%20quarter%20of%20Australians%20aged,serious%20but%20help%20is%20available.
[88]https://www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/pubs/rp/rp1819/Quick_Guides/MentalHealth
[89] https://www.phrma.org/Science/In-The-Pipeline/Medicines-in-Development
[90] https://www.beyondblue.org.au/media/statistics
[91] https://www.phrma.org/Science/In-The-Pipeline/Medicines-in-Development
[92] https://www.ausmed.com.au/cpd/articles/schizophrenia

- **27** for **substance use disorders**. Millions of Australians and their families are currently struggling with a range of substance use disorders, the majority of which go untreated. [93]The presence of co-occurring mental illness and substance use disorders can increase symptom severity, complicate treatment and create medication adherence challenges.
- **18** for **anxiety disorders**, which impacts one in four people – one in three women and one in five men – will experience anxiety at some stage during their lifetime. [94] There are several types of anxiety disorders, including, generalized anxiety disorder, panic disorder, phobia-related disorders (e.g., the fear of flying, heights or needles), social anxiety disorder and separation anxiety disorder.
- **17** for **attention-deficit/hyperactivity disorder (ADHD)**, which affects one in twenty Australians, that is 1.2 million people, but is frequently misunderstood and under-diagnosed.[95] It's estimated one in 20 children in Australia have ADHD. [96]ADHD is a brain disorder marked by an ongoing pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development.
- **11** for **bipolar disorders**, which affects 2.9% of Australians aged 16 and over, or 568,000 people. [97] Bipolar disorder, also known as manic-depressive illness, is a brain disorder that causes unusual shifts in mood, energy, activity levels and the ability to carry out day-to-day tasks.

The development of new and effective treatments for patients with mental illness is very challenging. But biopharmaceutical researchers are making strides in the world of mental illness by expanding the understanding of the underlying causes of these diseases and bringing about a new era in the treatment of mental illness. Now, more than ever, we understand that the appropriate treatment of mental health conditions, once they are first recognized, can change the trajectory of an individual's life for the better.[98]

[93] https://www.addictioncenter.com/addiction/addiction-in-australia/
[94] https://www.beyondblue.org.au/media/statistics
[95] https://www.adhdaustralia.org.au/about-adhd/what-is-attention-deficit-hyperactivity-disorder-adhd/#:~:text=ADHD%20(Attention%20Deficit%20Hyperactivity%20Disorder,co%2Docurring%20mental%20health%20conditions.
[96] https://www.rch.org.au/home/
[97] http://www.bipolaraustralia.org.au/bipolar-information/
[98] https://www.phrma.org/Science/In-The-Pipeline/Medicines-in-Development

Attachment 2: Medicines not available in Australia, but are available in other OECD countries

Registration Year	Product	Molecule	Therapy area	No. of other OECD countries reimbursed	Launched in Australia
2014	BRINTELLIX	VORTIOXETINE	Mental Health	3	Y
2014	BOSULIF	BOSUTINIB	Cancer	2	N
2014	XOFIGO	RADIUM RA-223	Cancer	1	Y
2015	OTEZLA	APREMILAST	Arthritis, Psoriasis	13	Y
2015	SUNVEPRA	ASUNAPREVIR	Hep C	3	N
2015	CYRAMZA	RAMUCIRUMAB	Cancer	18	N
2015	SYLVANT	SILTUXIMAB	Cancer	17	Y
2016	ZURAMPIC	LESINURAD	Arthritis, Psoriasis	8	N
2016	UPTRAVI	SELEXIPAG	Cardiovascular	16	N
2016	PRALUENT	ALIROCUMAB	Cardiovascular	15	N
2016	BELSOMRA	SUVOREXANT	Mental Health	2	Y
2016	FARYDAK	PANOBINOSTAT	Cancer	11	N
2016	EMPLICITI	ELOTUZUMAB	Cancer	13	N
2016	NINLARO	IXAZOMIB	Cancer	14	N
2017	CINQAIR	RESLIZUMAB	Respiratory	11	N
2017	SOLIQUA	INSULIN GLARGINE, LIXISENATIDE	Diabetes	1	N
2017	DARZALEX	DARATUMUMAB	Cancer	17	Y
2017	ONCASPAR	PEGASPARGASE	Cancer	7	Y
2018	DUPIXENT	DUPILUMAB	Arthritis, Psoriasis	8	N
2018	KEVZARA	SARILUMAB	Arthritis, Psoriasis	14	N
2018	ERLEADA	APALUTAMIDE	Cancer	6	Y
2018	IMFINZI	DURVALUMAB	Cancer	13	Y
2019	OZEMPIC	SEMAGLUTIDE	Diabetes	15	N
2019	MEKTOVI	BINIMETINIB	Cancer	14	N
2019	BRAFTOVI	ENCORAFENIB	Cancer	14	N
2019	ALUNBRIG	BRIGATINIB	Cancer	11	N
2019	NERLYNX	NERATINIB	Cancer	4	N
2019	VERZENIO	ABEMACICLIB	Cancer	13	N
2019	ZEJULA	NIRAPARIB	Cancer	12	N
2019	ULTOMIRIS	RAVULIZUMAB	Cancer	4	N
2019	POLIVY	POLATUZUMAB VEDOTIN	Cancer	1	N
2019	TALZENNA	TALAZOPARIB	Cancer	5	N
2019	CALQUENCE	ACALABRUTINIB	Cancer	1	N

Attachment 3: Reimbursement Practices in Other Countries

The Cancer Drug Fund in Great Britain has enabled faster access for cancer patients[99]

New medicines are automatically reimbursed in the National Health Service (NHS) for all approved indications upon receiving marketing authorization from the EMA or the Medicines and Healthcare Products Regulatory Agency if it is considered cost effective. Medicines that have been deemed not cost effective are unlikely to be prioritized for funding.

In England, Northern Ireland and Wales except Scotland, the National Institute for Health and Care Excellence's (NICE) recommendations are taken into consideration by funding bodies within those countries when deciding whether to fund the new medicine. NICE makes recommendations based on cost-effectiveness calculations using Quality Life Adjusted Years, and positive recommendations usually result in the medicine being funded.

The Cancer Drugs Fund (CDF) acts as a managed access pathway for new cancer medicines, and all new cancer medicines are referred to NICE for appraisal by the Department of Health and Social Care. A cancer medicine cannot be funded by CDF if is not recommended by NICE for routine NHS funding. The introduction of CDF has enabled patients to gain access to cancer medicines in the NHS at least 4 months earlier than was previously the case.

In Germany, a new medicine is reimbursed at market entry and reviewed in the second year after launch[100]

In Germany, new prescription medicines are automatically reimbursed following registration, but non-prescription medicines (with some exceptions) and lifestyle medicines are excluded from reimbursement. There are no reimbursement categories; medicines are either reimbursed or not.

On market entry, a new medicine is reimbursed at its launch price for the first year, pending the completion of an early benefit assessment. In the second year of launch, depending on the outcome of the early benefit assessment, the reimbursement price is determined either by:

1. compulsory rebate negotiations with the *GKV-Spitzenverband* (Federal Association of Health Insurance Funds) for medicines with an additional benefit versus a competitor.
2. reference price system where medicines with no additional benefit are reimbursed at the reference price, and patients pay the excess if they opt for a more expensive medicine. The prices are periodically reviewed by the *GKV-Spitzenverband*

The Gemeinsamer Bundesausschuss (Federal Joint Committee) can determine on an ad hoc basis to remove a medicine from reimbursement or restrict the medicine's reimbursed status so that the use of the medicine is deemed economically efficient.

In Japan, the Drug Pricing Organisation must determine if a new drug should be listed within 60 days of market authorisation[101]

For a new medicine to be eligible for reimbursement in Japan, it must have:

1. marketing authorisation from Pharmaceutical and Medical Devices Agency (PMDA);
2. included in the National Health Insurance reimbursement price list; and
3. not be specifically excluded from reimbursement (e.g. lifestyle products)

Medicines are reimbursed at the price listed on the National Health Insurance (NHI) reimbursement price list and applies equally to patients covered by the NHI, Employee Health Insurance (EHI) and Long-Life Medical Care System. Reimbursed drugs are subjected to price controls which included a price revision in 2018, resulting in an average 7.1 percent price cut on all reimbursed medicines.

[99] Source: IQVIA Pharma Pricing & Reimbursement Country Guide – UK December 2018

[100] Source: IQVIA Pharma Pricing & Reimbursement Country Guide – Germany September 2018

[101] Source: IQVIA Pharma Pricing & Reimbursement Country Guide – Japan June 2018

The speed of the reimbursement of Japan's system is a result of a timeframe requirement on the Drug Pricing Organisation. The Organisation must decide on whether to include a new medicine on the NHI reimbursement price list within 60 days of marketing authorisation, or up to 90 days if the manufacturer appeals the proposed reimbursement price.

Attachment 4: Data Exclusivity, Patent Notification and Market Sized Damages

What is data exclusivity?

Data exclusivity, sometimes referred to as regulatory data protection (RDP), prohibits third parties for a set period of time from using or relying upon an innovator's valuable clinical data to obtain regulatory approval for their product. Providing innovators with data exclusivity recognizes the time, costs, and uncertainty related to the research and development process for medicines and the substantial investment required to develop the clinical data needed for regulatory approval. Data exclusivity allows, for example, a biologic to be on the market for a set period before a biosimilar application can be approved based on the innovator's clinical data and protects against the uncertainties caused by patent challenges early in a product's life.

Patent notification and Market Sized Damages:

Australia has not implemented a system by which patent holders, as a matter of practice, receive advance notice of third-party applications for regulatory approval to be listed on the Australian Register for Therapeutics Goods (ARTG) by the Therapeutics Goods Administration (TGA) of potentially patent-infringing pharmaceutical products. Rather than notifying patent holders, generic manufacturers summarily certify their belief that their products do not infringe enforceable patents.

After TGA's approval, the generic/biosimilar product is usually quickly approved for reimbursement under the PBS leading to an immediate and irreversible statutory reduction of what the government pays to the innovator company of 25%. As the innovator has not had an adequate period to assess if the product infringes any of its patents, it is perversely forced into seeking injunctive relief to stop the product entering the market between the point of ARTG listing and the statutory price reduction to ensure its patent is protected. The litigation processes that subsequently ensue relate to clarifying whether a patent has been infringed. Such litigation is lengthy and costly and, as Medicines Australia has argued for many years, unnecessary if only timely notification was provided to the innovator to make this assessment earlier and provide a timely mechanism to resolve the issues with the TGA and generic/biosimilar company.

In addition, in cases of the court finding that a patent was not infringed, the Australian Government has sued innovators for damages attributed to a delay in the PBS price reduction while the patent dispute is being resolved. These so-called "market-sized damages" create significant uncertainty for pharmaceutical patent owners, who need to be able to rely on the rights conferred by granted patents (unless and until they are finally invalidated) to support the large investments needed to develop new medicines. It also undermines the rights of patent holders in Australia by introducing a strong disincentive to exercise their core right to enforce their intellectual property protections. It is also inconsistent with Australia's international commitments under the Australia – US Free Trade Agreement and the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).

Finally, there is no corresponding mechanism to compensate innovators for losses associated with the infringing product's premature launch and PBS price reduction. This policy sends a troubling signal that intellectual property protection can be undermined in an effort to drive down pharmaceutical prices. This also weakens Australia's attractiveness for biomedical foreign direct investment and discourages investment in new, lifesaving cures.

Attachment 5: Summary of Procedural Improvements to Align with International Best Practices

Summary of procedural improvements that could be implemented to benchmark with international best practice by remodelling regulatory workflows within the existing legislative timelines.

Item	US	EU	AU	Issue	Impact	Recommendations
Clinical Evaluation Resources						
Have sufficient internal resources to undertake clinical evaluations and do not rely on external resources	✓	✓	✗	High level of reliance on external clinical evaluators due to resource constraints.	Quality of external clinical evaluations can be poor due to lack of experience of evaluator in undertaking reviews or failure to understand regulatory requirements. This creates additional burden for Sponsors in having to address erroneous requests that are not relevant to a robust benefit risk assessment and can result in delays to approval and subsequent reimbursement	Continue to seek ways to reduce reliance on external evaluators or improve training and peer review through internal efficiencies and international work-sharing initiatives. Recent restructure to allow Delegates to focus on new product evaluations may reduce reliance on external evaluators over time.
Evaluation Process						
No requirement to pre-agree time for responses to questions prior to submission	✓	✓	✗	Requirement to pre-agree 30- or 60-day clock stop for questions to accommodate procurement of external evaluation resources at specific times	No flexibility to shorten or lengthen clock stop based on actual issues raised or number of questions received EU allows up to 90 days as default with option to extend to 180 days if justified.	Remodel workflow to provide more flexibility by reducing reliance on external clinical evaluation resources to accelerate approval process when only minor issues need to be addressed
Single integrated benefit/risk assessment performed	✓	✓	✗	Dual assessment based on initial evaluation reports and subsequent Delegate review of evaluation reports. This may result in new issues being raised late in the process that are reflected in the recommendations on benefit/risk and approvability in the Delegates Overview that differ from earlier evaluations.	Lack of early input from Delegate impacts predictability of outcomes due to new issues being raised late in the process. Time frames for responses are limited to 10 rather than the 30 or 60 working days allowed for questions raised during evaluation and a 6-page limit applies. This hinders Sponsors from being able to provide the most robust response even if data is available.	Remodel workflow to enable earlier input from Delegate to ensure questions are raised as part of list of questions to improve predictability of outcomes and support earlier planning of reimbursement applications.

Item	US	EU	AU	Issue	Impact	Recommendations
Questions raised during evaluation used to ensure all available data is considered to address any concerns relevant to benefit/risk	✓	✓	✗	Evaluation process does not require questions to be raised even when there are concerns identified in the evaluation report. A lack of clinical questions raised by TGA compared to international best practice is a major barrier to a streamlined and predictable evaluation that support early reimbursement	In the absence of questions being raised Sponsors have no formal procedural mechanism to provide relevant data. This can result in major issues being raised late in the process or requires case by case agreement to use 'out of process' approaches to enable submission of relevant information. Inconsistencies in ways of working across evaluation stream in such situations leads to further uncertainty for Sponsors.	Remodel workflow to ensure all questions relevant to a decision on approvability are asked as part of the list of questions to ensure Sponsors have the opportunity to address concerns.
Multiple rounds of questions allowed	✓	✓	✗	Process is designed based on a single list of questions	If concerns remain that a Sponsor would be able to address with available data, there is no mechanism in the process to provide this data. Case by case agreement to use 'out of process' approaches to enable submission of relevant information may be an option but inconsistencies in ways of working across evaluation stream in such situations leads to further uncertainty for Sponsors.	Remodel workflow to enable additional round of questions if required to address a major concern for which data are available
Responses to questions can include new or updated clinical data as part of the standard process	✓	✓	✗	Process restricts provision of data unless specific agreement in place	Data evaluated in Australia may diverge from that considered in other jurisdictions where process is more flexible to allow additional available data to be considered resulting in need for further resubmissions to achieve comparable outcomes which delays patient access	Remodel workflow to enable mutual cloak stops when appropriate to support provision of additional data and avoid need for delays in approval due to resubmission
Final evaluation reports represent agency position on data submitted and clearly articulate agency view position on approvability	✓	✓	✗	Uncertainty on approvability due to review of evaluation reports by Delegate which may lead to different recommendations to those in evaluation reports	Uncertainty around alignment of clinical evaluator, Delegate Overview and ACM on final indication wording may impact ability to finalise economic models required for reimbursement until final Delegate approval which delays access for patients	Remodel workflow to ensure Delegate input is reflected in final evaluation reports so no uncertainty for Sponsors on agency view on approvability allowing more predictable planning of reimbursement submissions

Item	US	EU	AU	Issue	Impact	Recommendations
Regulatory workflow does not result in delays in initiating reimbursement activities	✓	✓	✗	Due to uncertainty around alignment of Clinical Evaluator and Delegate, parallel processing of regulatory & reimbursement submissions is under-utilized. In addition, a bimonthly ACM cycle impacts availability of Delegates Overview as the trigger to initiate reimbursement	Delegates Overview received late in the process is commonly used as the trigger for reimbursement submissions resulting in delayed access for patients compared to parallel processing	Create joint TGA/PBAC pre-submission advice framework to ensure alignment of end to end processes and availability of Delegate Overview for cut off dates. Increase frequency of Delegates Overview to monthly cycle Remodel workflow to ensure Delegate input is reflected in final evaluation reports to create more certainty about final outcomes and encourage parallel processing to deliver earlier access for patients.
Advisory/Expert Committee Process						
No page limit for advisory/expert committee briefing documents	✓	✓	✗	The 6-page limit does not enable Sponsors to provide a robust response or adequately share available data if multiple complex issues raised	Inability to include all available data can negatively impact outcomes due to issues remaining that could have been addressed. This delays reimbursement while further negotiations are ongoing to resolve concerns.	Re-model workflow to incorporate clinical expert advice relevant to therapeutic area into evaluation process and enable Sponsors to provide expert input if required to address specific concerns.
Transparency of committee proceedings	✓	✓	✗	Sponsors do not receive information on ACM members involved in discussions for their products or the views of members on proposed ACM advice. Other jurisdictions have full transparency.	Lack of transparency does not align with other jurisdictions and significant additional regulatory burden and delays in approval can result when ACM members have views that differ from global standards of care that have be accepted in all other jurisdictions.	Improve transparency of ACM proceedings to match other jurisdictions.
Sponsor able to present and engage in dialogue with advisory body/committee	✓	✓	✗	ACM meetings are closed to Sponsors whereas Sponsor presentations including support from practicing clinical experts is standard practice in other jurisdictions	Inability to provide clarification to address concerns of committee members may have negative impact on recommendations or trigger a decision for the Sponsor to undergo an appeal process which delays access for patients whilst issues are resolved.	Re-model workflow to incorporate clinical expert advice relevant to therapeutic area into evaluation process and enable Sponsors to provide expert input if required to address specific concerns.

Item	US	EU	AU	Issue	Impact	Recommendations
Advisory body/committee comprises therapeutically aligned clinical experts and/or regulators	✓	✓	✗	ACM composition included broad range of experts whom may not be experts in therapeutic area	Recommendations may not align with established standards of care due to lack of knowledge in therapeutic area. Advice may be ignored by Delegate which makes value of committee process questionable	Ensure alignment of committee membership with therapeutic area of relevance