05. Investment In Clinical Trials Advances Innovation

Medicines Australia

Better health through research and innovation

Clinical Trials

Clinical trials are vital to the future of Australia's healthcare, as they contribute to the global efforts to find, discover and develop the latest breakthrough medicines, vaccines and biotherapeutics.

Clinical trials also provide significant spill over benefits to Australian patients. They facilitate earlier and faster access to new, breakthrough treatments, bring health professionals together to deliver better care for patients, and encourage patients to actively participate in their care.

Summary

Australia has many advantages as a place to conduct clinical trials. This is in large part because Australia is home to some of the world's best researchers and health professionals and boasts a world-class research infrastructure, a stable socio-political environment, and high clinical and research standards that ensure confidence in the scientific conclusions reached by clinical trials conducted in Australia. Australia generally has a robust intellectual property system and a tier one regulatory framework. The Australian Government is also committed to improving the clinical trials environment and has invested considerable effort and resources accordingly. These are all factors that have contributed to the strong growth of investment in clinical trials in Australia by global biopharmaceutical and medical technology companies over the past three decades.

Investing in Australia's clinical trials ensures a robust workforce, better health outcomes for patients and an increased body of scientific knowledge and medical innovation. Clinical trials provide opportunities for Australian scientists and medical researchers to be at the forefront of solving the major health challenges of our time.

Medicines Australia has strongly encouraged successive Australian Governments to implement reforms that would further enhance Australia's attractiveness as a destination for clinical trials.

Challenge	Solution
Regulatory arrangements for clinical trials are overly complex and variable across the States and Territories leading to unnecessary delays in the initiation of multicentred clinical trial sites.	Federal, State and Territory Governments (through the COAG Health Council) to work together, and with industry, to find agreement for regulatory harmonisation and mutual recognition that optimises clinical trial initiation and shortens commencement times.
Challenge	Solution
Patient recruitment processes and timelines for clinical trials are comparably slow which may lead to trial closure and reduces Australia's access to clinical trial programmes.	Government to work with industry and other clinical trial stakeholders to enhance patient access to clinical trials through improved coordination; better community promotion of the value of clinical trials; digital information platforms to optimise awareness of clinical trial opportunities; ongoing harmonisation of patient records; and enhanced tele-health initiatives to improve patient recruitment in remote and regional areas.
Challenge	Solution
To optimise Australia's competitiveness and ensure Australia is a preferred destination to conduct clinical trials, leading to a measurable increase in clinical trial activity in Australia.	Government to work with industry on developing a mutually agreed, coordinated long-term strategy for Clinical Trials including consideration of a Parliamentary Friends of Clinical Trials.

Overview

According to MTPConnect's report, Clinical Trials in Australia, the most recent data from 2015 showed that 1,360 clinical trials were started that year (including 473 industry sponsored trials) supporting approximately 7,000 jobs - a $1.1 billion in investment.[1]

Australia needs to maintain a top position as a preferred destination for clinical trial investment due to the positive spillover effects on Australian patients and the broader economy. This is threatened by slow initiation times for clinical trial sites, often due to fragmented governance across the States and Territories. Additionally, patient recruitment can be poor due to lack of community and clinician awareness, and costs frequently vary across sites. In some instances, costs are significantly higher than comparable sites and competing countries. These issues present increasing challenges, compared to other rapidly advancing regional jurisdictions who are competing for clinical trials.

A clinical trial is a scientific study, or an organised test, of medicines and new treatment options involving patient and non-patient human volunteers. Clinical trials confirm whether medicines are safe and effective to introduce as new treatments for a disease or condition. Clinical trials are also necessary to determine whether an existing medicine can be safely and effectively used for other diseases and/or conditions. Clinical trials are also used in comparative effectiveness trials in the health system to ensure optimal and evidence-based therapeutic approaches are applied and cost-effectiveness is demonstrated.

The benefits for trial participants include early access to promising new treatments in Australia, concentrated specialist care and greater self-involvement in their own care. Other flow-on benefits include the exposure, education and experience of Australian clinicians and health professionals to new and cutting edge technology, which also allows the introduction of new treatments and care regimes that may increase the health and productivity of all Australians.

Why Do We Need Clinical Trials?

> **Clinical trials are essential to the development of new interventions.**

For example, without clinical trials, we cannot properly determine whether new medicines developed in the laboratory or by using animal models are effective or safe, or whether a diagnostic test works properly in a clinical setting. This is because computer simulation and animal testing can only tell us so much about how a new treatment might work and are no substitute for testing in a living human body.

Clinical trials are critically important to Australia because:

- Results from clinical trials can lead to the development of new medicines that can assist Australians to treat and manage their condition(s).
- Patients can gain early access to new medicines/treatment options not otherwise available, at no cost. In some instances, a clinical trial is the treatment of last hope for some patients.
- Participation in clinical trials can improve the lives of thousands more people suffering from various medical conditions if the safety and efficacy of a treatment proves beneficial.
- Finding new treatments can help reduce the burden of some of our most challenging diseases such as cancer, cardiovascular diseases and central nervous system diseases.
- They generate new valuable insights for science and research, through development of knowledge that can be important when treating future patients.
- They create employment in our research organisations, universities and hospitals.
- They provide clinicians with early access to and experience of the latest innovative medicines, treatments and technologies.
- They are used to inform decisions by the Therapeutic Goods Administration (TGA) and the Pharmaceutical Benefits Advisory Committee (PBAC) to register and subsidise a medicine.

While medicines are extensively tested in laboratories, these tests can only predict how a medicine will act under theoretical conditions. To thoroughly understand how a new medicine actually performs in humans, it needs to be tested on people, including those affected by the disease the medicine is designed to treat.

During clinical trials, participants are closely monitored to examine how a drug is absorbed and excreted; to establish the correct dosage of the medicine; to understand how safe it is; to observe (and counter) what side effects may occur, and to confirm if it is effective in treating the disease for which it has been developed. Clinical trials may also compare, or combine, the new treatment with other available options.

Member Case Studies

Bristol-Myers Squibb (BMS)

- BMS recognises the strength and capability of local clinical researchers and includes Australia in the top six countries for participation in global clinical trials of its industry-leading bio-pharmaceuticals pipeline.
- In 2017, BMS invested more than $33 million in clinical trials in Australia.
- In 2017 BMS supported 65 clinical trials in Australia, with more than 1300 patients taking part in BMS trials in partnership with more than 100 academic research institutes, laboratories, clinical and other organisations.

Amgen has conducted clinical trials in Australia for more than 30 years, and rates Australia as one of the top medical study locations outside the United States. As one of the world's largest biotechnology companies, Amgen partners with Australian research institutes and investigators, taking advantage of leading-edge biotechnology research for the benefit of patients.

Through its significant clinical presence, Amgen Australia conducts on average two first-in-human studies every year, and almost half of its clinical trial activity is in early phase research (Phase I and II). In 2018, Amgen conducted 49 different studies at 75 sites across Australia and New Zealand, involving 665 patients.

Amgen Australia invests around $30-35 million in local research and development annually, which represents around 10 percent of its sales.

The company reaps the benefits of accessing Australia's wide range of scientific talent and Australia's medical infrastructure.

Clinical trials are generally initiated by a 'trial sponsor', which can be a medicine company (for new medicines) or they may be initiated by medical specialists and doctors in the health system (comparative effectiveness studies). Sponsors come from a wide range of organisations. They include:

- Medicines companies, either solely or jointly with other research institutions such as universities and hospitals;
- Private research institutes (such as the Garvan Institute; or the Walter and Eliza Hall Institute of Medical Research) under a grant, commonly through the Government's National Health & Medical Research Council (NHMRC) or from public or private donations; and
- Publicly funded research organisations such as universities and teaching hospitals.

In Australia each clinical trial is overseen by a doctor. The clinical trial team includes doctors and nurses as well as pharmacists and other health care professionals. The clinical trial team is responsible for checking the health status of the participants at the beginning of the trial, monitoring them during the trial, and staying in touch with them for a period of time after the clinical trial has been completed.

Table 1: Australia's relative competitive position: drivers and impediments

Drivers	Impediments
• Medical experts/research with global standing and experienced staff • Quality of local research capability and output • Ethnically diverse population • Specialised and dedicated infrastructure	• Complex arrangements to establish a trial including variable arrangements for clinical governance and ethics approval • Lower recruitment rates • High trial costs • Inconsistent processes between states and territories • Lack of coordinated long term strategy

The above set of drivers and impediments illustrates that, although Australia has many attributes which provide a strong competitive position for industry sponsored trials, unless Australia is prepared to continue to reform the trials environment to remain an attractive location for global clinical trials and develop a long term strategy, Australia runs the risk of significant competition from lower cost geographies such as the Asia Pacific and Latin America. As international competition intensifies, Australia will have to address these challenges.

Challenge	Solution
Regulatory arrangements for clinical trials are overly complex and variable across the States and Territories leading to unnecessary delays in the initiation of multicentred clinical trial sites.	Federal, State and Territory Governments (through the COAG Health Council) to work together, and with industry, to find agreement for regulatory harmonisation and mutual recognition that optimises clinical trial initiation and shortens commencement times.

Australia's clinical trials environment is complex and can vary considerably across Australia's study sites, States and Territories. Inconsistent regulatory and governance processes, slow start up times and poor patient recruitment are regularly identified by clinical trial sponsors as one of the key reasons why Australia is losing its competitive edge against other countries.

Despite ongoing bipartisan commitment to reforms, the time it takes to start a clinical trial in Australia is not getting shorter. Industry surveys continue to cite the lengthening research governance approval timelines as one of the main contributors.[2] Previous studies have shown that, on average, research governance reviews add 49 calendar days to approval times. As an example of the increasing complexity; despite supporting the concept of single ethical approval via national mutual acceptance, the three largest states have introduced two, stand-alone, ethics and governance IT systems.

The practical impact is that clinical trial applications must be entered twice, once into each system, if a sponsor wishes to open sites in all three states.

Other countries are taking the lead on supporting clinical trials. For example, in July 2016 the new European regulation on clinical trials commenced. These regulations require a single application for a clinical trial, via a European portal to the European Medicines Agency (EMA), which will be evaluated in consultation by all member states involved in the trial. Timelines for evaluation and approval are to be harmonised across all the member states in Europe.

Other comparable countries to Australia, such as Canada, have efficient and responsive regulatory systems for clinical trials. These include many mechanisms to expedite clinical trial start-up times.

There will always be complexities in Australia because of the shared responsibility for healthcare between the Australian Federal Government and State and Territory Governments. As shown overseas, driving greater efficiency in the clinical trials environment can be achieved. With increasingly fierce competition for attracting clinical trial investment, now more than ever we need to keep pace with international standards and best practice models for clinical trial approvals.

Ensuring efficient establishment of trials and competitive timelines for enrolling patients is critical to improving health outcomes and the overall productivity of the economy. States that maintain they should have regulatory control over certain clinical trial activities could still harmonise legislation at the State level to support greater national consistency. This would be particularly timely given that State Governments have already agreed to work in good faith with the Australian Government to improve the clinical trials environment.[3]

Medicines Australia welcomes the bipartisan commitment to improve harmonisation of clinical trial regulations and governance between the States and Territories. We look forward to working with the Government to take a position for such harmonisation to a meeting of the COAG Health Council.

Challenge	Solution
Patient recruitment processes and timelines for clinical trials are comparably slow which may lead to trial closure and reduces Australia's access to clinical trial programmes.	Government to work with industry and other clinical trial stakeholders to enhance patient access to clinical trials through improved coordination; better community promotion of the value of clinical trials; digital information platforms to optimise awareness of clinical trial opportunities; ongoing harmonisation of patient records; and enhanced tele-health initiatives to improve patient recruitment in remote and regional areas.

One of the barriers to initiating more clinical trials in Australia lies in the difficulty in recruiting suitable patients to enrol in clinical trials. The barriers to patient recruitment include:

- a lack of patient and clinician awareness of clinical trials;
- inappropriate or ineffective communication methods to raise awareness;
- identifying the right patients;
- length and complexity of application processes and a lack of harmonization of patient records and regulatory frameworks; and
- inability to access clinical trials in remote and rural regions.

Australia, with its smaller and dispersed population, often finds it difficult to meet patient recruitment targets. The recruitment process can also be prohibitively costly to the trial sponsor, if a large-scale advertising or outreach campaign is required. In addition, a protracted recruitment period for a trial will result in higher salary costs for the Institutions, as research nurses are required for longer periods to support a clinical trial. In some cases, clinical trial sites are closed, and access to trials lost, if recruitment is too slow. Potentially eligible patients who would benefit from participating in a clinical trial may have a low awareness of the value of clinical trial or may be unsure how to access a trial. There is also an opportunity to improve access for rural and remote Australian patients to clinical trials.

The medicines industry is tightly regulated with regard to information it can share publicly on proposed clinical trials. These barriers may lead to delays in commencing trials, early termination or small sample sizes that make it difficult to draw meaningful conclusions and are another potential disincentive to initiating trials in Australia.

It is proposed that an Australian coordinating body for clinical trials be responsible for identifying and implementing initiatives that will enhance patient recruitment for clinical trials. This may involve raising the awareness of the public in general of clinical trials; supporting programs such as tele-trials to improve rural and remote patient access to clinical trials; raising awareness amongst patients and healthcare professionals on how to locate clinical trials, through improving digital information platforms promoting vehicles such as the Australian clinical trials portal www.australianclinicaltrials.gov.au; conducting nationally coordinated media campaigns; and providing materials and support to States/Territories who wish to increase patient involvement in clinical trials locally.

Challenge	Solution
To optimise Australia's competitiveness and ensure Australia is a preferred destination to conduct clinical trials, leading to a measurable increase in clinical trial activity in Australia.	**Government to work with industry on developing a mutually agreed, coordinated long-term strategy for Clinical Trials including consideration of a Parliamentary Friends of Clinical Trials.**

Australia is globally recognised as having some of the best scientists and research infrastructure which gives us an important strategic advantage. But we are facing fierce international competition for clinical trial investment and over a ten-year period, overall levels of clinical trial activity have been steady at best.

There are a range of factors which impact Australia's competitiveness when benchmarked against global rivals. For example, lengthy start up times owing to Australia's complex clinical governance and ethics approvals can add significant time and cost to establishing a trial and enrolling patients. Additionally, our smaller population can lead to slower uptake of trials and lower patient enrolments per trial site leading to a higher per patient cost. Australia is also more challenged in terms of referrals of patients between trial sites, notwithstanding our well-developed health system.[4]

In MTPConnect's 2017 report, Clinical Trials in Australia: The Economic Profile and Competitive Advantage of the Sector states that:

"These factors have implications on the economics of a site, as the set-up cost is a fixed cost that can only be spread across a limited number of patients. Limited numbers of participants per site also implies that in some therapeutic areas the competition for the same patients among trial sponsors is high. Additionally, given that consistent costing has not been applied throughout the sector, clinical trial costing remains complex and variable."

A national coordinating body could develop a long-term strategy ensuring the Australian clinical research environment is efficient and operates to world's best practice, to benefit patients and improve national health. This would be achieved by benchmarking at a national level Australia's performance in key areas, such as timeliness of start-up (ethics and governance), patient recruitment, and monitoring the levels of clinical trial activity across Australia. This would allow the development of a "roadmap" for the expansion of investment in clinical trials in Australia.

The strategy would also encompass such issues as workforce development, identification of best practices, promotion of Australia as a clinical trials destination, ongoing streamlining of governance processes, monitoring and benchmarking costs of clinical trials and appropriate charging methodologies in Australia versus our relevant competitors, continuing integration of E-health, digital platforms and harmonised patient records, state of the infrastructure including investment, and identification of new areas of opportunity.

Given the high degree of bipartisan support for clinical trials by political parties, parliamentarians in the 46th Australian Parliament could establish a new parliamentary friendship group. The goal of the group would to be to raise greater awareness amongst parliamentarians and the wider community about the benefits of clinical trials. Establishment of the Parliamentary Clinical Trials Friendship Group would also provide a forum for discussion on opportunities to improve the clinical trial environment. It would also help build a mutual understanding of the economic opportunities clinical trials create and the health benefits it helps to deliver for Australians. The group could be supported by Medicines Australia, Research Australia, AusBiotech and the Australian Clinical Trials Alliance, with peak bodies offering to help educate members through research, briefings and other information.

1 MTP Connect, Clinical Trials in Australia. https://www.mtpconnect.org.au/clinicaltrials

2 PwC Pharma Industry Survey, 2015, Challenges and Change, a report on the Australian pharmaceutical industry. Available at: https://www.pwc.com.au/industry/healthcare/assets/challengesa-and-changes-final.pdf;

3 Council of Australian Governments Health Council, April 2016, CHC Communique. Available at: http://www.coaghealthcouncil.gov.au/Announcements/ArtMID/527/ArticleID/92/CHC-Communique-8-April-2016;

4 MTPConnect, Clinical Trials in Australia: The Economic Profile and Competitive Advantage of the Sector, https://www.mtpconnect.org.au/images/MTPConnect%202017%20Clinical%20Trials%20in%20Australia%20Report.pdf.pdf

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