Clinical Trials in Australia:

THE ECONOMIC PROFILE AND COMPETITIVE ADVANTAGE OF THE SECTOR

June 2017

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Foreword

Clinical trials are an integral part of the safe and reliable development of new treatments and refinement of existing treatments. They are vital in maintaining the health and wellbeing of society. The conduct of clinical trials in Australia attracts sizeable investment from international companies and exposes Australian clinical staff to world-leading healthcare practices. Through both commercial and public spend, clinical trials in Australia support thousands of jobs within the research and healthcare systems including doctors, nurses, researchers, administrators and many more across a vibrant ecosystem. Clinical trials ultimately serve patients through early access to new treatments and improving standards of care. As such, clinical trials play an important part in the Australian economy and society.

The Australian clinical trials sector has developed considerably in recent years, with changes in structure and increases in sector activity levels. This has been underpinned by a large number of initiatives encompassing all stakeholders.

With this report, MTPConnect aims to give a holistic and comprehensive overview of the current state of the sector, outlining how the conduct of clinical trials makes a significant contribution to Australian economic activity. It also outlines Australia's competitive position in the world to inform local and international stakeholders on the attractiveness of Australia as a destination to conduct clinical trials.

MTPConnect, alongside many local sector participants, believes that Australia is well positioned to continue delivering efficient and effective trials for sponsors and to be a pioneer in emerging innovative clinical trials. We hope that this report and its account of the sector will provide the impetus and fact base needed to pursue opportunities and initiatives that ensure Australia maintains and improves on, its current position as a world-leading clinical trial destination. This will ultimately strengthen the outlook and position of clinical trials in Australia and continue to build on the benefits the sector provides to all stakeholders.

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Executive summary

Clinical trials are an integral part of the research and development of new treatments, interventions or tests, and the refinement of existing standards of care and clinical practices. As such, they are vital to the future of healthcare. Within the broad field of clinical trials there are two distinct but interdependent segments: industry sponsored trials (largely focused on the development and testing of new medicines or devices) and non-industry sponsored trials such as investigator-initiated trials (typically focused on optimising the use of existing treatments and clinical processes within the health system). Both segments rely heavily on the presence of a skilled, supportive and efficient clinical trials ecosystem in Australia and both contribute to the significant value that the sector creates for the wider economy and society.

In economic terms, the value generated directly through the conduct of clinical trials is referred to as the **economic activity** of the sector, and it consists of the level of clinical trials activity in Australia (i.e. number of trials) and the corresponding funding that supports it. While precise figures vary across data sets, sources suggest that approximately 1,360 new clinical trials were commenced in Australia in 2015.[1] Clinical trial volumes have experienced strong growth since 2010, with Australia outperforming the majority of competitor nations (Figure 17). Total direct expenditure for ongoing clinical trials was estimated at $1.1 billion in 2015.[2] For comparison, the OECD estimates that Australian expenditure on health and medical research & development (R&D) was approximately $4.3 billion in 2008 (the most recent year data was available).[3] An estimated $930 million of this funding for clinical trials is provided by commercial entities and the large majority of this can be attributed to international inbound investment. The estimated total expenditure supports approximately 6,900 highly skilled staff across commercial and clinical entities.[4] The investment into clinical trials also includes expenditure for medicines and other healthcare costs for participants on trials, which is largely borne by the industry sponsors.[5]

Figure 1 Australia's clinical trial sector at a glance

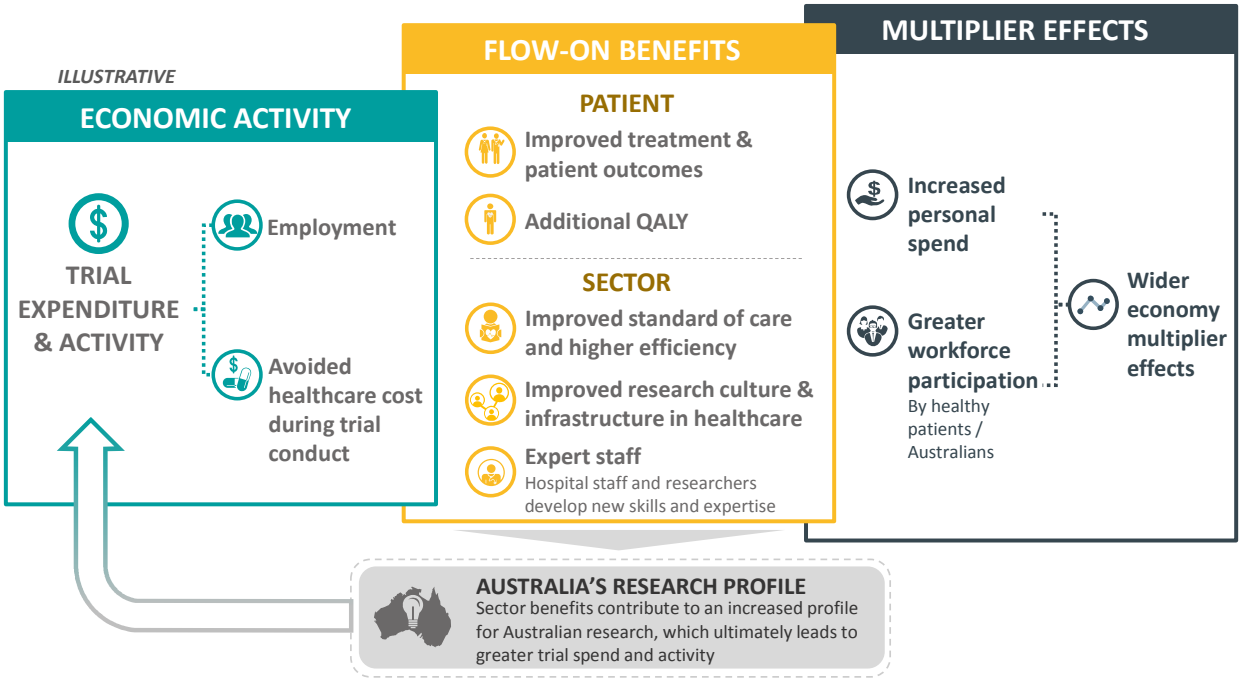
[1] This figure is estimated with an error range of plus or minus 10%, due to limitations on the accuracy and completeness of the underlying data (as detailed in section 2.3.1)
[2] Including funding from industry sponsors, NHMRC, MRIs, and through Clinical Trials Networks, as detailed in section 3.2.1
[3] OECD stats data; Gross domestic expenditure; Includes business, government, higher education and private non-profit expenditure on Medical and Health Science R&D
[4] According to ACTA, Clinical Trials Networks have approx. 10,000 members but many participate in clinical trials part-time only
[5] Clinical Trials Action Group, Clinically Competitive: Boosting the Business of Clinical Trials in Australia, 2011

Clinical trials also generate a range of **flow-on benefits**. These include benefits for trial participants such as early access to improved treatment in Australia and ultimately an increase in the number of quality-adjusted life years (QALY) across subsets of the population that participate in trials. There are also flow-on benefits beyond the participants directly involved in clinical trials, such as the introduction of new treatments or improvements to care regimes that raise the health and productivity of all Australians, and these spill over into the wider society and healthcare community, generating additional value for Australia. A detailed assessment and quantification of these healthcare benefits are out of scope for this report.

Other flow-on benefits accrue to the medical technology, biotechnology, pharmaceutical and healthcare sectors in the form of training and access to up-to-date technology, techniques and treatments for clinical and research staff. Clinical trials also provide Australian healthcare professionals with the opportunity to work with and develop expertise in the latest innovative medicines and devices, increasing their international profile. Establishing an improved research culture in hospitals and the funding of hospital-level infrastructure that supports other forms of medical research outside of clinical trials are also considered flow-on benefits. These benefits support the creation of a cohesive research ecosystem that local industry can leverage to conduct clinical trials and commercialise their products, acting as catalysts for the overall development of the local medical technologies, biotechnologies and pharmaceuticals sector.

Furthermore, the economic activity of the sector and flow-on benefits ultimately generate **economic multiplier effects**, such as personal expenditure and contribution to taxation by clinical trial sector staff in the economy, and the availability of healthier individuals in the workforce.

Figure 2 The value of clinical trials in Australia



The scope and scale of value that clinical trials generate in Australia cannot be fully evaluated without understanding Australia's position in the global marketplace. Many markets compete for clinical trial activity (especially industry sponsored trials) as these trials contribute significantly to their respective local healthcare systems and economy, as discussed above. Between 2012 and 2015, the number of clinical trials registered in Australia grew by approximately 2% p.a., with trials involving a device growing by approximately 10% year-over-year. 2% p.a. growth for clinical trials is in line with the global average, while 10% p.a. growth for device trials is significantly above the global average. While estimates of industry contributions vary by data source, 350-500 out of a total of approximately 1,360 of clinical trials in Australia are industry sponsored trials and at least 31% of trials are conducted as part of trials with recruitment in other countries as well (i.e. global trials).[6] These industry trials are important drivers of inbound investment, accounting for approximately 75% of total annual sector expenditure. It is thus important to consider Australia's relative position, competitive strengths and ability to compete for clinical trials in the global marketplace. Consultation with local and global industry experts have uncovered key drivers of and impediments to Australia's competitive position in the global clinical trials market.

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

DRIVERS	IMPEDIMENTS
• Medical experts / research with global standing and experienced trial staff • Quality of local research capability and output • Rapid trial start up process: Therapeutic Goods Administration Clinical Trial Notification (CTN) scheme and streamlined ethics • Specialised and dedicated infrastructure • Comparable cost[7], including the value of the research & development tax incentive	• Complex site governance: individual site governance process is highly variable and requires further streamlining • Low participant recruitment numbers per site which in turn drives higher cost per patient • High trial cost for certain sub-sectors • A need to invest to develop capability in specialised, high risk and innovative trials to remain a leading trial destination

The implication of these drivers and impediments is that Australia has a strong competitive position in conducting industry sponsored clinical trials in complex therapeutic areas (e.g. oncology), in trials with complex design (e.g. adaptive trial design), and in early stage trials (e.g. Phase I drug trials and feasibility / first time in human medical device trials [FTIH]). High standards of internationally recognised research, leading medical experts with global standing, infrastructure quality, as well as high standards of care are considered critical to sponsors of such types of trials. In these trial types, Australia is considered a leader in the region and is generally compared on par with other trial markets that feature advanced health systems such as Europe and North America. In trials with lower complexity in design or that require features such as large patient pools, Australia is increasingly rivalled by competitors with better access to larger patient pools and lower cost bases from Asia Pacific, Eastern Europe or Latin America.

[6] Based on L.E.K. analysis of Australian New Zealand Clinical Trials Registry (ANZCTR) data (including additional entries registered on clinicaltrials.gov) and NAS data

[7] At long run exchange rate averages

As international competition for clinical trials intensifies, it will be critical for Australia to address the impediments outlined above to ensure continued growth in the sector.

Over the last decade, Australian sector participants have recognised this challenge and have not been standing still. A wide range of initiatives have been actioned or are in progress to address past reform recommendations such as those outlined in the Clinical Trials Action Group (CTAG) report.[8] Progress has been made across each of the recommendation areas and benefits in some areas are already being realised (e.g. streamlined and more rapid ethics approval), while other areas are still a work in progress (e.g. consistent costing and generating awareness to improve participant recruitment).

These initiatives have been key in maintaining competitiveness, especially by improving processes towards more efficient conduct of clinical trials. However, further structural improvements and a focus on Australia's strengths in clinical trials are required to unlock a step-change in growth for the sector. MTPConnect, in line with other initiatives, has identified a number of priority areas for further improvement under two overarching themes that relate to the scope of this report:

1. **Improving the attractiveness of Australia as a clinical trials destination. There are many areas that need to be addressed to meet this goal. There are three in particular that MTPConnect considers high priorities for the entire sector**

    a. continuing to optimise efficiency in the conduct of clinical trials, in particular through governance improvements

    b. enhancing patient numbers per trial and site economics by improving recruitment and retention

    c. investing to build deeper capabilities in innovative and novel clinical trial types, including adaptive trial design, complex first time in human (FTIH) trials and trials involving translational medicine. These areas are future opportunities for growth and will allow Australia to compete in sub-sectors that are less price sensitive than the standard, high volume trials.

2. **Enhancing transparency / visibility of the state of the clinical trials sector.**

    Currently no sector wide data sets exist to accurately track the number of clinical trials, the economic contribution of the entire sector, or performance levels in the conduct of clinical trials (especially in high growth sectors such as medical device trials). Without this sector view, it is challenging to track progress and drive accountability and improvements over time. MTPConnect recommends the development of a holistic data set to be reported annually, or every two years, drawing on data that already exists and filling gaps to enable these goals to be met.

A large body of work is already underway to address these issues and improve the Australian clinical trials environment, with a view to improving health outcomes and increasing international investment in Australia (see section 5.2). MTPConnect acknowledges and supports

[8] Clinical Trials Action Group, Clinically Competitive: Boosting the Business of Clinical Trials in Australia, 2011

the work already being undertaken in many of these areas by public and private sector participants, and calls for greater collaboration between the public and private sectors to further advance these priorities.

By building on areas of strength and pursuing further structural improvement, Australia could realise a considerable increase in annual expenditure by the sector. Additional funding to achieve these objectives will also come from Government sources such as the Medical Research Future Fund (MRFF). According to the 2017-18 Federal Budget, more than $30 million of initial disbursements are expected to be directed towards the conduct of clinical trials over the next four years. The Hon. Greg Hunt, the Minister for Health, has indicated that funds will be allocated to support research into public health and therapeutic areas that tackle the highest burden of disease, as well as to the Australian Clinical Trials Alliance (ACTA), National Health and Medical Research Council (NHMRC) fellowship schemes, and State and Territory infrastructure.[9]

In that light, if Australia can maintain its trials growth rate and significantly improve on structural issues such as participant recruitment, it can surpass $2 billion of annual expenditure in the next 10 years and create more than 6,000 new high skilled jobs in a sustainable sector, driving broader health and economic benefits for Australians.

[9] Media release by the Hon. Greg Hunt, "Delivering $33 million to help fund our next medical breakthrough" (19/05/2017)

1 Context

Clinical trials have long been an important bedrock for local clinical research, providing participants with access to new treatments and contributing to the wider Australian society. Recent years have seen considerable attention given to the Australian clinical trials sector through calls for reform and initiatives to maintain Australia's status as an attractive destination in a highly competitive and evolving global marketplace. While significant progress has been made, the Australian clinical trials environment remains complex, generally uncoordinated and fragmented. In addition, both sector participants and the broader public generally lack a clear understanding of the current state of the sector locally or a relative assessment of Australia's position in the global marketplace.

The purpose of this report is to provide a holistic picture of the Australian clinical trials sector, and the level of economic activity and the economic value derived from the conduct of trials. In the past, several reports have described segments or sub-sets of the overall sector, e.g. activity at a state level, or non-commercial clinical trial economic activity.[10] A comprehensive national view of the economic and other benefits of the full suite of clinical trial activity in Australia is important to inform sector participants, policy makers and other stakeholders, both within and outside of Australia, on the value of the sector and opportunities for growth.

This report provides a fact base consisting of:

- a holistic overview of the sector, the broad range of participants and the level of clinical trial activity;
- an outline of the value derived from the conduct of clinical trials and quantification of the economic impact of conducting trials in Australia;
- a perspective on the competitive advantage of Australia in the global marketplace of clinical trial sites;
- a summary of initiatives completed or underway that are seeking to implement reforms to enhance Australia's conduct of trials and its competitiveness;
- suggested priority areas of initiatives to further strengthen the sector; and
- an outlook on potential future growth of the sector.

This report is one of several current or recent reports exploring the Australian clinical trials landscape. Together they provide a comprehensive and complementary view of the sector.[11]

The report has been prepared by consolidating research available in the public domain and complementing it with input from government agencies and departments, industry associations, sector participants and stakeholders, including a number of international commercial decision makers. MTPConnect would like to thank all the sector stakeholders who have contributed their time and input to the report.

[10] For example see ACTA's Report on the Activities & Achievements of Clinical Trials Networks in Australia 2004-2014, 2015

[11] See also: Clinical Trials Jurisdictional Working Group Framework for National Aggregate Statistics Second Activity Report on Clinical Trials in Australian Public Health Institutions, 2017; Federal Department of Health, Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials, 2016; ACTA, Economic evaluation of investigator-initiated clinical trials conducted by networks, 2017; Australian Government Department of Health, Analysis of Recently Conducted Clinical Trials, 2015

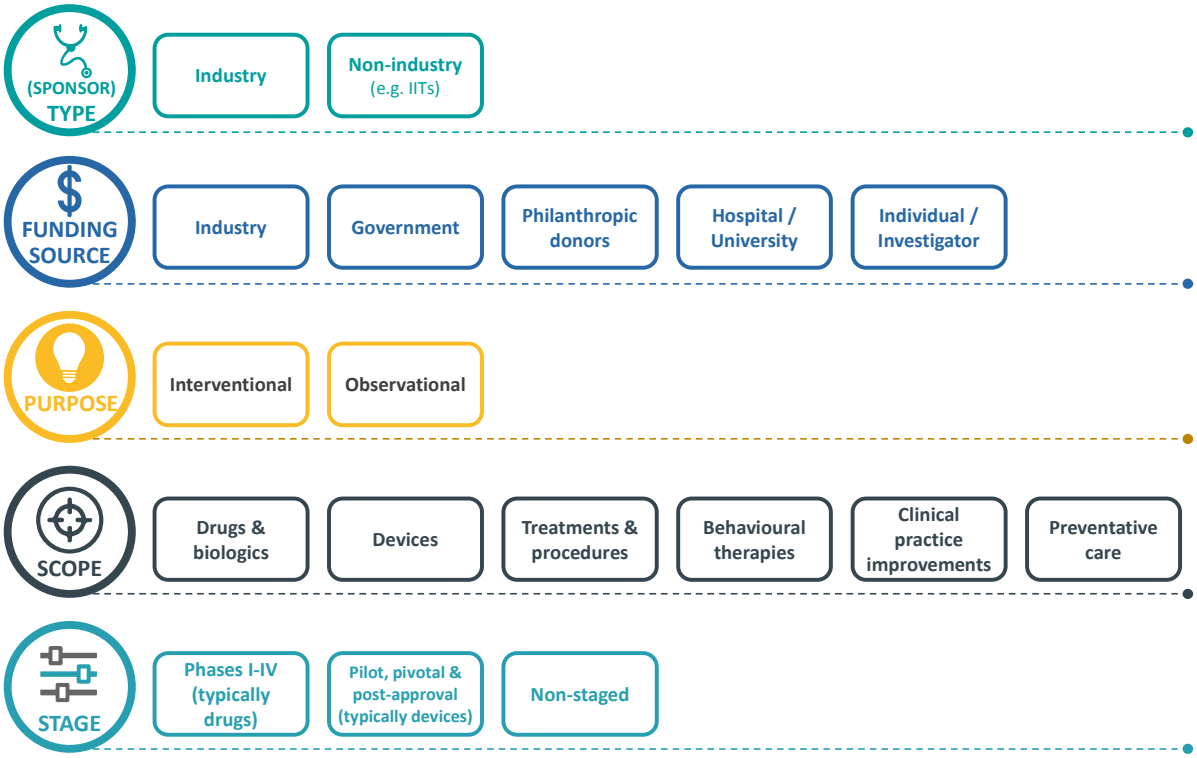
2 The Australian clinical trial sector overview

2.1 The definition of clinical trials

Clinical trials are an integral part of the research & development (R&D) of new treatments, interventions or tests, and the refinement of existing standards of care and clinical practices. As such, clinical trials are the primary process by which preventive, diagnostic and therapeutic strategies are evaluated with human subject. [12] Studies generate evidence to inform stakeholders about the degrees of safety, effectiveness, efficacy and cost-effectiveness of the investigated strategy on health outcomes.

Clinical trials can take many forms, with widely varying features and characteristics depending on the unique circumstance of each study. They can be segmented based on the purpose of the underlying sponsor entity, their primary source of funding, their intended trial purpose, the scope of their investigation and the stage structure they follow.

Figure 3 Clinical trial segmentations



[12] Calif, R M, Zarin, D A, Kramer, JM, et al (2012) Characteristics of Clinical Trials Registered in ClinicalTrials.gov 2007-2010. The Journal of the American Medical Association, 307(17) 1838-1847; The World Health Organisation defines clinical trials for the purpose of registration as: *"any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes"*

Clinical trials are commonly categorised based on **sponsor** type: either industry sponsored trials and non-industry sponsored trials or investigator-initiated trials (IITs), which incorporate a range of trials including academic trials, GP trials or collaborative group trials. Industry trials are sponsored, funded and conducted by medical technology, biotechnology and pharmaceutical (MTP) companies that aim to commercialise the underlying intellectual property (either directly or through partnerships / licensing). These trials are conducted to satisfy regulatory requirements for approval of new interventions and products.

The large majority of non-industry trials are conducted for the public good by investigating clinically relevant research questions to identify the best treatment irrespective of its commercial value. These types of trials may evaluate already licensed products or common procedures for comparative effectiveness in the Australian health system, testing a product in routine clinical practice instead of controlled environments, or exploring new uses for old drugs that are no longer on patent.

Further, a large number of non-industry trials investigate procedures or protocols in the broader context of model of care and implementation science.[13] Trials in this category can relate to outpatient care within allied health services e.g. different recovery procedures for patients post-operation, or the most effective physiotherapy treatments for a hip replacement patient, or they may be interventional studies that do not involve a drug or a device e.g. the effect of listening to music on dementia patients. Whilst these trials do not typically commence in the pursuit of commercial gain, they often result in changes to standards of care or treatment methods, ultimately improving patient outcomes and cost effectiveness across the health system.

Non-industry trials are associated with a broader set of funding sources. While some of these trials are funded by industry, they more commonly rely on government (public) funding, philanthropic donations and funding from institutions (universities, hospitals). A small sub-set of these trials may also be self-funded by the sponsoring institution or the investigator.

In terms of **purpose**, clinical trials are segmented into interventional trials and observational studies. In the former, participants receive or do not receive medical or health interventions for researchers to evaluate the effects on health or biomedical outcomes.[14] In observational studies, participants of a study group are assessed for biomedical or health outcomes in a non-controlled setting, where the investigator does not assign specific interventions to specific groups of participants.[15]

[13] Based on L.E.K. and MTPConnect interviews with sector participants

[14] An intervention in this context is a diagnostic, therapeutic or other clinical strategy intending to affect a health outcome (Definition based on NHMRC Australian Clinical Trials - *https://www.australianclinicaltrials.gov.au/what-clinical-trial*)

[15] National Institute of Health (NIH) & clinicaltrials.gov glossary - *www.nih.gov/health-information/nih-clinical-research-trials-you/glossary-common-terms* & *clinicaltrials.gov/ct2/about-studies/glossary*

The **scope** of clinical trials captures the different categories and types of interventions. They include, but are not restricted to, experimental drugs, vaccines, cells and other biological products, medical devices, surgical, radiologic and other medical treatments and procedures, psychotherapeutic and behavioural therapies, process-of-care changes or clinical practice improvements (i.e. implementation science trials) and preventive care.[16,17]

Certain clinical trial types can be further segmented into **stages**. Studies investigating biomedical interventions such as biological or pharmaceutical compounds are categorised by a four phase model. Medical device trials generally follow a different staging structure from pilot studies through to post approval or marketing studies.[18]

2.2 Overview and role of sector participants

The conduct of clinical trials in Australia involves a number of key sector participants – each undertaking distinct roles and activities. These groups are generally defined as MTP companies; service providers such as Contract Research Organisations (CROs); and clinical research affiliated organisations such as Medical Research Institutes (MRIs), public and private hospitals, universities, private clinical trial sites, Clinical Trials Networks and GP networks (see Figure 4).

Figure 4 Sector organisations[19]

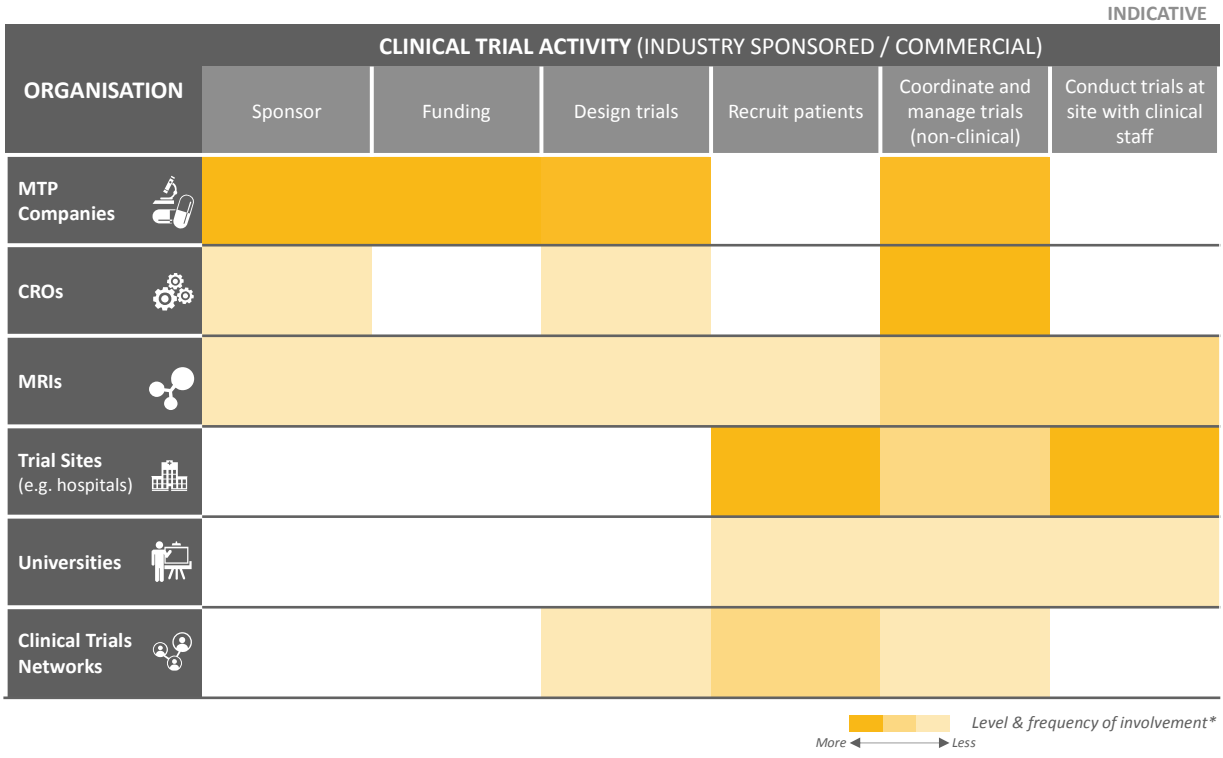
MTP COMPANIES (INDUSTRY)	• Medical technology, biotechnology and pharmaceutical companies are the main sponsors of clinical trials in Australia in value terms. They can be segmented into multi-national companies and local or regional firms • Biotechnology and pharmaceutical companies typically outsource the conduct of clinical trials to CROs and other research service providers. Medical technology companies typically conduct them in-house
CONTRACT RESEARCH ORGANISATIONS (CROs)	• CROs are service providers that design, plan and manage clinical trials on behalf of sponsors (typically MTP companies) • CROs range from small, niche local providers to large, full service multi national companies
MEDICAL RESEARCH INSTITUTES (MRIs)	• MRIs are institutes focused solely on medical research, including the conduct of clinical trials across the value chain in Australia. They are typically specialised in one or more therapy areas • MRIs are often intertwined with hospitals, universities and Clinical Trials Networks • In 2015, AAMRI reported 46 MRI member organisations (of which 38 were independent) and 1,220 active trials at AAMRI Member Institutes

[16] World Health Organization Glossary - *www.who.int/ictrp/glossary/en*
[17] National Health and Medical Research Council - *www.australianclinicaltrials.gov.au/what-clinical-trial*
[18] Further details are provided in Appendix B.
[19] L.E.K. / MTPConnect interviews with sector participants, early 2017

TRIAL SITES / UNITS (Public/private hospitals, private clinics, specialised units, GP practice)	● The main role of a trial site is to host trials and provide clinical staff for the conduct of trials on site ● Hospitals are involved in clinical trials both as sponsors, and in recruiting, treating and monitoring patients in trials on behalf of other sponsors. Private clinics are less likely to sponsor trials, however they are often involved in recruiting patients and conducting trials
UNIVERSITIES	● While not usually trial sites, universities are major contributors to medical research in Australia ● They are typically involved in early stage trials where the risk is too great for MTP companies or the level of investment is not prohibitive, or in trials relating to clinical practice (rather than new drugs or discoveries)
CLINICAL TRIALS NETWORKS	● A Clinical Trials Network is a group of researchers, clinicians and academics who share infrastructure to conduct multi-centre clinical trials and facilitate knowledge-sharing between researchers in a field ● They are virtual and do not have physical labs or buildings ● In 2014, ACTA identified 37 Clinical Trials Networks in Australia and analysed data from 34 of them. The 34 Clinical Trials Networks reported 588 clinical trials ongoing in 2014

These entities deploy across the 'value chain' of clinical trials, taking on various roles, depending on their expertise, their objective, the type of trial (e.g. industry sponsored vs. non-industry sponsored trials) and the context of the individual trial. Organisational involvement across the value chain is shown for industry sponsored trials in Figure 5 and for IITS in Figure 6.

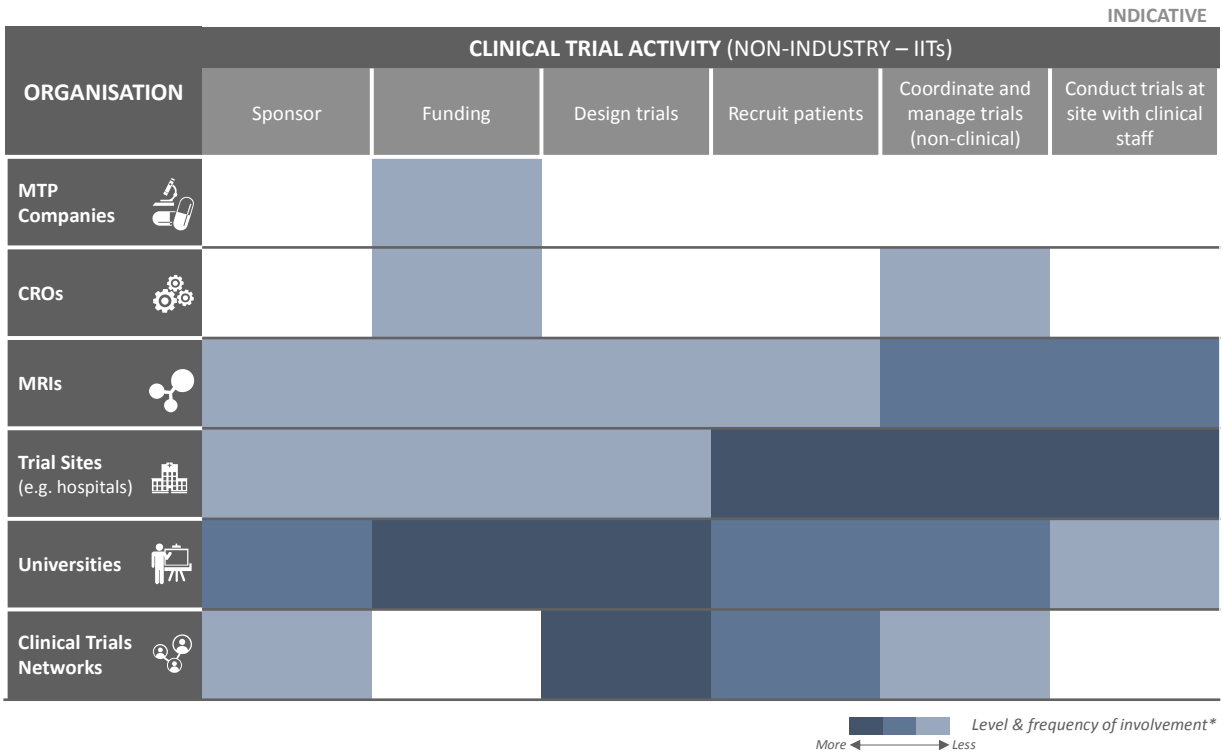
Figure 5 Organisation involvement in industry sponsored trials



Notes: * Level and frequency of involvement assessed qualitatively through research and discussions with sector participants

For industry sponsored or commercial trials, the sponsor and funder is by definition almost always an MTP company. Industry sponsors typically commission clinical trials in order to ensure a safe product and obtain the relevant approvals before commercialising a new drug or therapeutic. However, clinical trials are typically conducted by separate entities, with sponsors having no direct involvement at the trial site. The design of trials as well as the coordination and management of all non-clinical aspects are either conducted by the sponsor or by a CRO. Recruitment and the clinical conduct of the trial is generally managed by a hospital or MRI and their staff, with a 2011 survey estimating that 72% of all trials are being conducted in hospitals and 15% in MRIs.[20]

Figure 6 Organisation involvement in non-industry sponsored trials



Notes: * Level and frequency of involvement assessed qualitatively through research and discussions with sector participants

Non-industry sponsored trials are generally sponsored by the entity or person that developed / owns the trial protocol (e.g. MRIs, hospitals, universities, principal investigators). This sponsor is responsible for the entire management of the trial. These trials typically involve a combination of funding from various government sources and the sponsor entity. The recruitment, clinical and non-clinical management, tend to be undertaken in hospitals or MRIs. Clinical Trials Networks, universities, MRIs and hospitals will often co-locate and collaborate to conduct trials and thus are present across the value chain.

[20] Pharmaceuticals Industry Council, 2011 Survey of Privately Funded Clinical Research Activity, 2012

2.3 Clinical trials activity in Australia

2.3.1 Overview of the clinical trial data landscape

Clinical trial activity can be characterised across various dimensions such as number of trials, number of sites participating in a year, or number of patients that are recruited into active clinical trials. Clinical trial activity in Australia is not tracked centrally in a consistent and comprehensive way. Activity is tracked by multiple distributed and fragmented data registries, with no single data source capturing all clinical trial activity in Australia. This can partially be traced to the fragmented funding and sponsor landscape as well as a lack of legislation requiring centralised registration or authorising central tracking. Sources of trial activity can be segmented into regulatory trial notification (e.g. Therapeutic Goods Administration's [TGA] CTN scheme), trial registries (e.g. Australian New Zealand Clinical Trials Registry [ANZCTR]) and jurisdictional ethics and research governance data (e.g. the Clinical Trials Jurisdictional Working Group's [CTJWG] National Aggregate Statistics [NAS] report).[21]

The definition of clinical trials can vary significantly by source type, impacting the breadth of each source's respective data. These differences reflect the variation in intended purpose, methodology and structure of the datasets. See Appendix C. for clinical trial definitions by source type.

For the purposes of this report, MTPConnect has compared findings from several data sources, across source types, to provide a comprehensive view of available sources and activity in Australia. It is acknowledged that each data source has strengths and limitations, based on the intended purpose, methodology and the structure of the underlying dataset. Collaborative efforts are underway through the Council of Australian Governments (COAG) Health Council and jurisdictional health departments to improve provision of clinical trial metrics in the longer term.[22]

[21] Clinical Trials Jurisdictional Working Group Framework for National Aggregate Statistics Second Activity Report on Clinical Trials in Australian Public Health Institutions (2015-16)

[22] Clinical Trials Jurisdictional Working Group Framework for National Aggregate Statistics Second Activity Report on Clinical Trials in Australian Public Health Institutions (2015-16)

Table 2 High-level summary of clinical trial data sources

Source type	Source description
Regulatory trial notification	**Clinical Trial Notification / Exemption scheme (CTN / CTX)** The TGA indirectly tracks clinical activity via the CTN / CTX scheme. Any clinical study that investigates an unapproved therapeutic good or use of an existing good in an unapproved indication has to formally notify the TGA and supply it with key trial details for approval. This includes drugs, biologicals and medical devices across industry sponsored trials and non-industry sponsored trials, but excludes any trials that only use approved drugs and devices in approved indications, or that don't involve drugs or devices. Thus it only captures a subset of trial activity within Australia. It has to be noted that Clinical Trial Notification (CTN) numbers do not necessarily translate directly into actual clinical trial activity as there may be multiple CTNs per trial or trials may not go ahead. Nonetheless this represents the most comprehensive source for trials of unapproved therapeutic goods that is available to MTPConnect.
Trial registries[23]	**Clinicaltrials.gov** A US-based clinical trials registry open for all trial and intervention types. Registration for trial types is generally voluntary. However, registration is a legislative requirement for all US trials governed by FDAAA801 regulation (e.g. trials with sites in the US, trials investigating products regulated under the US Food and Drug Administration (FDA), trials funded by US organisations). Commercial entities seeking marketing authorisation of their products by the FDA are required to register on clinicaltrials.gov. **ANZCTR** (Australian New Zealand Clinical Trials Registry) Voluntary registry covering the full range of trial and intervention types. It also incorporates a data feed from clinicaltrials.gov to supplement locally registered trials in Australia and New Zealand. Both databases offer different sets of studies due to differences in geographic focus and legislative requirements. Therefore, the combination may provide a good indication of public and private trial activity when filtered to Australian trials. In 2017, the ANZCTR staff have estimated that it captures 75-80% of clinical trial activity in Australia.[24] **WHO International Clinical Trials Registry Platform (ICTRP)** The World Health Organization (WHO) hosts a search portal that aggregates a number of clinical trial registries around the world. It is not a registry itself and only aggregates select fields from its constituent registries. While this implies that it captures relevant activity in Australia such as ANZCTR, clinicaltrials.gov and others, reconciliation between its constituents is not complete.

[23] Trials are typically only registered on one registry, however some duplication does exist
[24] L.E.K. / MTPConnect interviews with ANZCTR Management, 2017

Jurisdictional ethics and research governance data	**CTJWG National Aggregate Statistics (NAS)** The Clinical Trials Jurisdictional Working Group (CTJWG) recently began an initiative to develop a national dataset on clinical trials and activity in Australia. This initiative demonstrates the commitment of all Australian governments to strengthening the clinical trial sector's performance and reflects the metrics that industry have indicated are important. The corresponding NAS reports compile and analyse data from public hospitals across Australia. The NAS leverages the Australian Research Ethics Database (AU RED) and the National Mutual Acceptance (NMA) ethics scheme to link cross-jurisdictional ethics applications, eliminate duplicates and provide a high standard of data integrity. NAS reports on clinical trial activity and other performance indicators such as start up time. The 2015-16 report features jurisdictional data from New South Wales, the Northern Territory, Queensland, South Australia and Victoria. All jurisdictions are actively working towards contributing to future NAS reports, and provision of the complete set of NAS metrics, including recruitment and investment estimates.

For the purpose of this report, the ANZCTR dataset (including its feed from clinicaltrials.gov) and the NAS report were used to assess clinical trial activity in Australia. These sources are the most comprehensive available, but were each designed for a unique purpose and face limitations based on research methodology and data coverage that need to be considered when interpreting the presented data.

Limitations to the ANZCTR data include:

- the voluntary nature of trial registration and updates. While commercially funded studies are mandated to register by the Ethics Committee other studies are not, meaning that some studies may not be captured in the data. The voluntary nature can also lead to duplicate or out of date records, including trials that were withdrawn / stopped but the corresponding ANZCTR entry was not updated to reflect this. While ANZCTR makes every effort to identify and correct these, some errors are likely to persist;[25]
- growth in overall trial volume from 2010 to 2015 is likely a combination of real volume growth and increased compliance for registration of trials on ANZCTR. According to the ANZCTR, increased compliance appears to be less of a driver of activity since 2012.

In addition, the following limitations of the NAS data must be considered:

- the NAS currently captures trials in public health institutions, but does not capture trials conducted in private health organisations, universities or primary care settings (except where the primary care setting is a trial site for a trial with a main primary administering base in a public hospital) as these are not linked into the data systems used by public health institutions;

[25] To illustrate this issue, for its 2015 'Report on the Activities & Achievements of Clinical Trials Networks in Australia', ACTA conducted a detailed comparison of ANZCTR with its own records of activity of Clinical Trial Networks. This analysis suggested that ANZCTR overstated the actual number of trials in 2014 by approximately 10% (primarily IITs), due to duplicates, separate entries for sub-trials and trials which were entered but not initiated. For this report, L.E.K. has systematically removed a small number of duplicate records between clinicaltrials.gov and ANZCTR, based on unique ID numbers. However, L.E.K. has not conducted more detailed data cleaning.

- the NAS does not include observational studies, except for Phase IV or other Post Marketing Surveillance (PMS) activities;
- it may under-represent clinical trials in publically funded hospitals as some jurisdictions currently have limited capacity to report in NAS format (i.e. ACT, Tasmania and Western Australia) and / or have incomplete datasets for single-site trials;
- time series data is not yet available, as only one edition of the NAS has been publicly released. However, the intention is to develop future editions of the NAS.

ANZCTR and the NAS each report on a variety of trial dimensions, including total number of clinical trials started per year, activity by segment, time series data and overall study start up timelines. Each data source used in this report captures trials at a different point in trial start up. ANZCTR tracks the time of anticipated or actual start date, the NAS the point of ethics approval application and TGA the point of trial notification. Table 3 below outlines the dimensions across the two datasets that were available for analysis at the time of preparation of this report.

Table 3 Summary of dimensions by data set

Data source	Number of trials started	Activity by segment				Historical time series	Start up times
		Study type	Intervention type	Phase	Sponsor type		
ANZCTR	✓	✓	✓	✓	✓	✓	
NAS	✓			✓	✓		✓

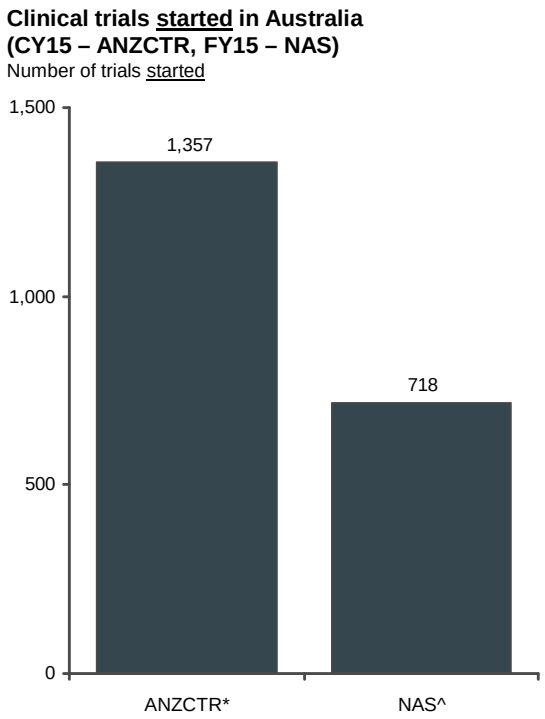
The outcome of the analysis of each of these dimensions is presented in the following sections.

Analysis of the TGA dataset has also ^been undertaken to provide a top-line view of clinical trials activity over the last six years and a detailed view of CTNs in 2016. A view on this has been provided in Appendix F. Analysis of TGA Data.

2.3.2 Clinical trial activity in Australia

As discussed above, clinical trial activity in Australia is not tracked exhaustively. Figure 7 shows that according to the ANZCTR registry, 1,357 trials were started in 2015. Considering the limitations outlined in the previous section, this will include some level of duplicated or outdated entries but also does not capture an undefined number of trials due to the voluntary nature of registration. The NAS report suggests that in FY2015, 718 trials were started in public hospitals in the included jurisdictions. While this is an accurate representation of these sites, it underestimates the total level of activity in Australia due to its data coverage, which excludes private and non-hospital sites, and the exclusion of certain observational studies from the NAS (as discussed above).

Figure 7 Total clinical trials started in Australia, by source[26]



Note: * Excludes 'Withdrawn' trials and duplicate entries. Where trials had a 'NULL' actual start date, the anticipated start date was used. ^Jurisdictions represented are: New South Wales, Northern Territory, Queensland, South Australia and Victoria. The 'Sponsor Type' field is not reported in some jurisdiction for individual trials
Source: ANZCTR and ClinicalTrials.gov – combined by ANZCTR; NAS; L.E.K. analysis

In summary, this analysis reinforces the observation that it is currently not feasible to know with accuracy the actual level of activity in Australia in any given year. Interviews with ANZCTR and ACTA indicate that the true number of clinical trials in Australia is likely to be around 1,360, with an error rate of plus or minus 10%. There are two factors that influence the accuracy of ANZCTR clinical trial numbers:

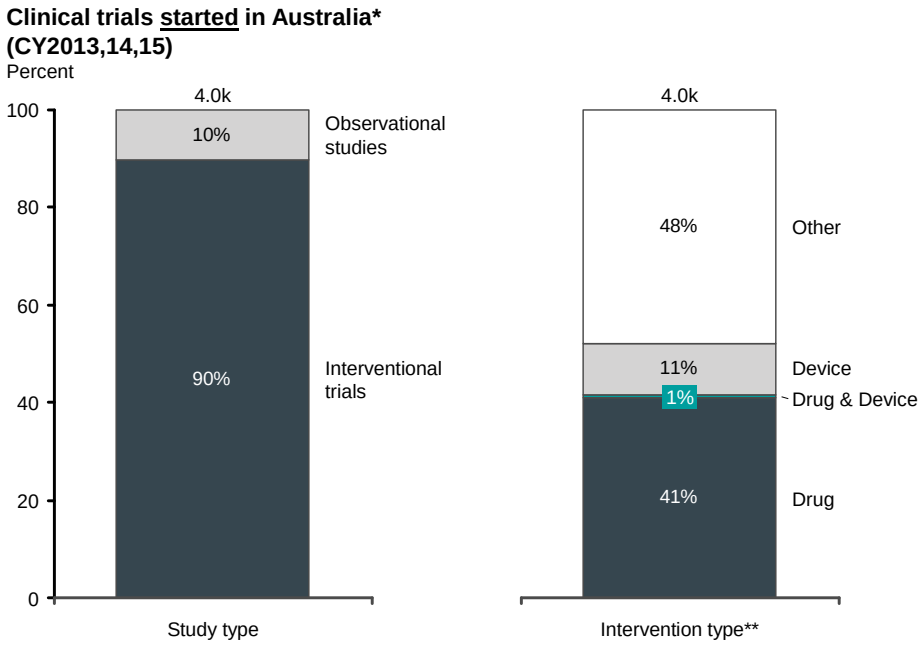
- ANZCTR coverage of total trial activity: ANZCTR estimates that it currently covers 75-80% of all trial activity in Australia, which suggests that actual trial numbers are higher than what is captured in ANZCTR[27]
- The presence of duplicates and incorrect data in the ANZCTR dataset: ACTA conducted a detailed comparison of ANZCTR with their own records of activity of Clinical Trial Networks. This analysis suggested that ANZCTR is overstating the actual number of trials by approximately 10%, due to duplicates, separate entries for sub-trials and trials which were entered but not initiated.[28] This duplication is expected to primarily affect non-industry sponsored trials since the number of industry-sponsored trials align fairly closely across the ANZCTR, NAS and TGA datasets (once adjusted for the coverage of each data set).

[26] Each data source used in this report captures trials at a different point in trial start up. ANZCTR tracks the time of anticipated or actual start date and the NAS tracks the point of ethics approval application
[27] L.E.K. / MTPConnect interviews with ANZCTR Management, 2017
[28] ACTA, Report on the Activities & Achievements of Clinical Trials Networks in Australia 2004-2014, 2015

2.3.3 Clinical trial activity by study and intervention type

According to the ANZCTR, between 2013 and 2015, approximately 4,000 trials commenced in Australia, with the large majority being registered as interventional trials, i.e. trials that intend to directly affect health outcomes for participants. As Figure 8 shows, around 50% of trials that started in this period do not involve a drug or device, suggesting a large number of trials are for non-biological procedures or methods of care, clinical practice improvements or preventative care. Drug trials are identified as the largest intervention type, with 41% share of clinical trials.

Figure 8 Summary of clinical trials started in Australia, by type[29]



Note: * Excludes 'Withdrawn' trials and duplicate entries. Where trials had a 'NULL' actual start date, the anticipated start date was used; ** Drug includes all 'drug' or 'biological' intervention types only (excluding any 'device' intervention types). Device includes 'device' intervention types only (excluding any 'drug' or 'biological' intervention types). Drug & Device includes both 'drug' and/or 'biological' and 'device' intervention types. Other includes: 'Behavioral', 'Procedure', 'Genetic', ' Radiation', 'Dietary Supplement', (not exhaustive) and trials where no intervention type was specified
Source: ANZCTR and ClinicalTrials.gov – combined by ANZCTR; L.E.K. analysis

2.3.4 Clinical trial activity by phase

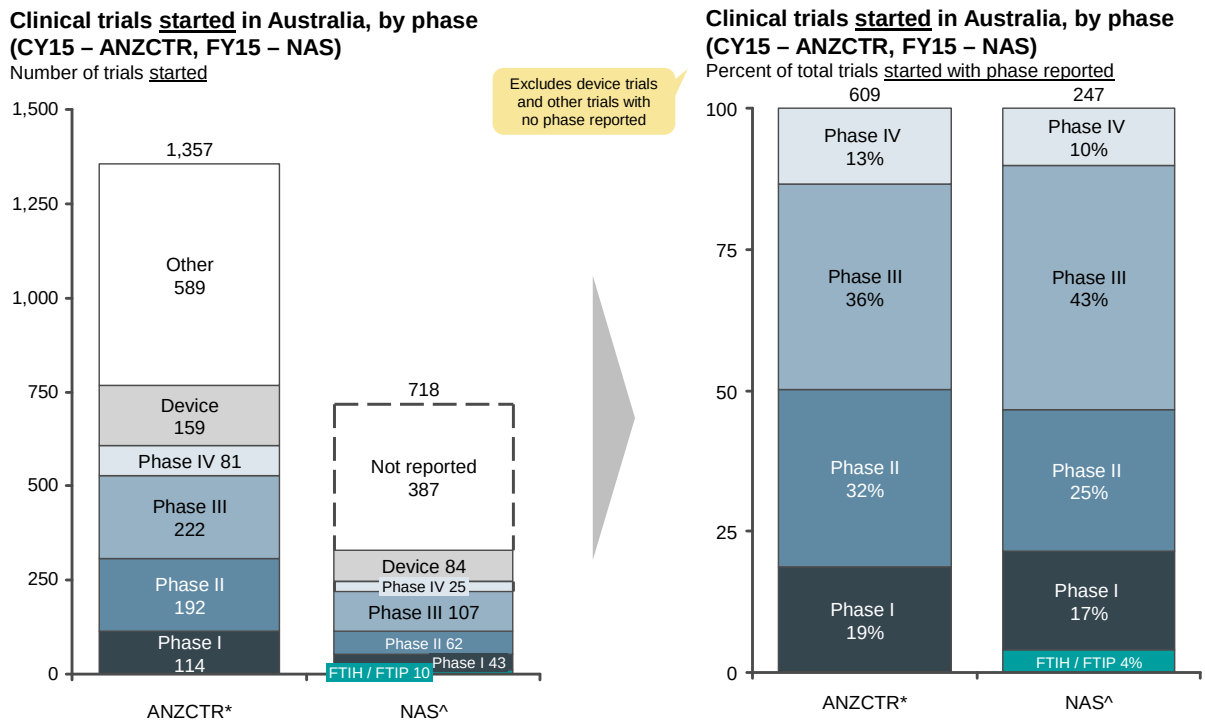
The ANZCTR and the NAS both track a variety of activity segments for clinical trials in Australia. Drug trials typically follow a phased approach and are reported in Phases I-IV. Device trials typically do not have phases recorded as they are staged according to a different system. Out of 1,357 reported trials, the ANZCTR reports 609 trials (45%) with phase recorded. Similarly, of 718 trials, the NAS identifies 237 (33%) with a phase classification.[30]

For trials that report a phase, the percentage breakdown by phase is similar between the ANZCTR and the NAS despite differing coverage and absolute totals. The ANZCTR and the NAS

[29] This analysis uses data from ANZCTR aggregated across 2013, 2014 and 2015 to account for variations across individual years
[30] Analysis excludes device trials and trials with no phase reported

suggest that, for trials with phase reported, 17-19% are in Phase I, 25-32% in Phase II, 36-43% in Phase III and 10-13% in Phase IV.

Figure 9 Summary of clinical trials started in Australia, by phase



Note: * Excludes 'Withdrawn' trials and duplicate entries. Where trials had a 'NULL' actual start date, the anticipated start date was used. Phase I includes 'Phase 0', Phase II includes 'Phase 1 / Phase 2', Phase III includes 'Phase 2 / Phase 3' and Phase IV includes 'Phase 3 / Phase 4'. Other includes 'Not Applicable' or 'N/A', and trials with no phase indicated. Device includes all trials with a "Device" intervention type only – no breakdown of device trial phases is available; ^Jurisdictions represented are: New South Wales, Northern Territory, Queensland, South Australia and Victoria. The 'Sponsor Type' field is not reported in some jurisdiction for individual trials

Source: ANZCTR and ClinicalTrials.gov – combined by ANZCTR; NAS; L.E.K. analysis

The TGA's 2016 CTN statistics are within a similar range to the ANZCTR and the NAS. Of those with a phased structure, 22% are reported in Phase 1, 26% in Phase II, 36% in Phase III and 16% in Phase IV.[31]

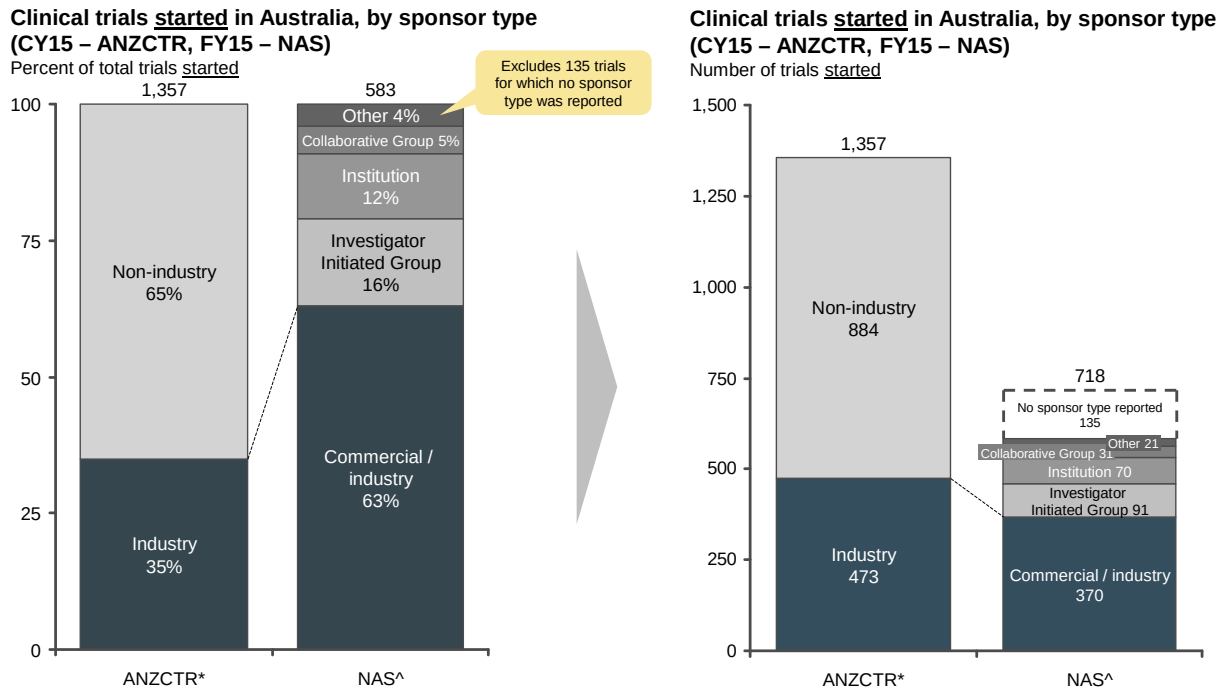
2.3.5 Clinical trial activity by sponsor type

Both ANZCTR and the NAS report trials by sponsor type. The reported figures are different in relative terms, primarily due to the underlying coverage of the two data sets. According to the ANZCTR, around one third of all trials are sponsored by industry entities. However, the NAS reports that 63% of trials are sponsored by industry.

While the percentages differ between the two datasets, the absolute numbers of industry sponsored trials are similar. The ANZCTR identifies 473 industry sponsored trials in CY15 while the NAS identifies 370 in FY15. Again, the difference in coverage (i.e. trials in private health organisations and three jurisdictions were not included in NAS in the reporting period) may account for the discrepancy in this case.

[31] Please refer to Appendix F. Analysis of TGA data. Excludes device trials and trials with no phase reported

Figure 10 Summary of clinical trials started in Australia, by sponsorship type



Note: * Excludes 'Withdrawn' trials and duplicate entries. Where trials had a 'NULL' actual start date, the anticipated start date was used. Industry sponsored includes: 'Industry' and 'Commercial sector/Industry'. Non-industry sponsored includes: 'Government body', 'NIH', 'U.S. Fed', 'Individual', 'University', 'Hospital', 'Other', 'Other Collaborative groups', 'Charities/Societies/Foundations' and trials where no sponsorship type was specified; ^Jurisdictions represented are: New South Wales, Northern Territory, Queensland, South Australia and Victoria. The 'Sponsor Type' field is not reported in some jurisdiction for individual trials

Source: ANZCTR and ClinicalTrials.gov – combined by ANZCTR; NAS; L.E.K. analysis

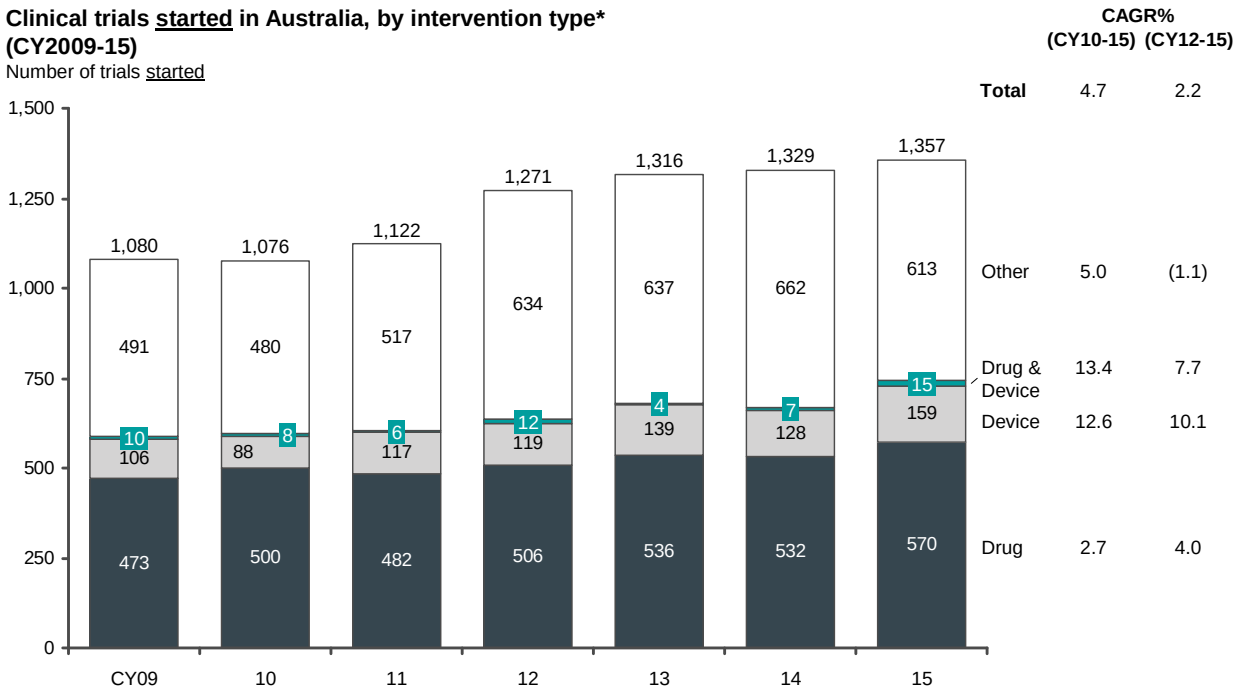
2.3.6 Clinical trial activity over time

The data lodged in the ANZCTR indicates that between 2010 and 2015, the total volume of clinical trials starting in Australia has grown at a compound annual growth rate (CAGR) of approximately 4.7% p.a., slowing to approximately 2.2% p.a. from 2012 to 2015 (Figure 11).

Trials with 'other' intervention types such as non-biological procedures or methods of care, clinical practice improvements or preventative care have grown over this period. However, this growth in part may also be due to increased registration compliance, following the recommendation in 2004 from the International Committee of Medical Journal Editors and subsequent policies and laws that all trials be registered prospectively in order for their results to be published. This recommendation has been gradually adopted by journals and researchers.

In addition, the ANZCTR data suggests that trials that involve devices have seen strong growth (approximately 13% p.a.) between 2010 and 2015 from a relatively low base. Drug trials have shown steady growth of 3% to 4% p.a. which is expected to be reflective of the true level of trial activity due to consistent compliance in registration of trials since at least 2012.

Figure 11 Number of new trials commencing in Australia, by intervention type



Note: * Excludes 'Withdrawn' trials and duplicate entries. Where trials had a 'NULL' actual start date, the anticipated start date was used; ** Drug includes all 'drug' or 'biological' intervention types only (excluding any 'device' intervention types). Device includes 'device' intervention types only (excluding any 'drug' or 'biological' intervention types). Drug & Device includes both 'drug' and/or 'biological' and 'device' intervention types. Other includes: 'Behavioral', 'Procedure', 'Genetic', ' Radiation', 'Dietary Supplement', (not exhaustive) and trials where no intervention type was specified

Source: ANZCTR and ClinicalTrials.gov – combined by ANZCTR; L.E.K. analysis

Growth in trial numbers can also be considered by phase. Historically, the majority of clinical trials in Australia that follow the four phase approach (primarily drug trials) have been Phase II or III trials. Early stage trials have experienced stronger growth than late stage trials in recent years, likely reflecting the excellent reputation of Australian early stage specialised units. As noted above, device trials have grown strongly since 2010.

Table 4 Clinical trial activity growth, by intervention type and phase

	Drug						Device	Drug & Device[32]	Other	Total
	Phase I	Phase II	Phase III	Phase IV	Other	Drug Total				
Growth (p.a. 2010-15)	6.6%	3.2%	2.7%	(1.2%)	(2.3%)	**2.7%**	12.6%	13.4%	5.0%	**4.7%**

Source: ANZCTR; L.E.K. analysis

From a sponsor and trial type perspective, the majority of growth in number of trials was driven by industry sponsors, specifically from 2012 to 2015.[33]

[32] ANZCTR indicates that some Drug & Device trials also report phase data. For the purposes of the above phase analysis, only drug trials have been included

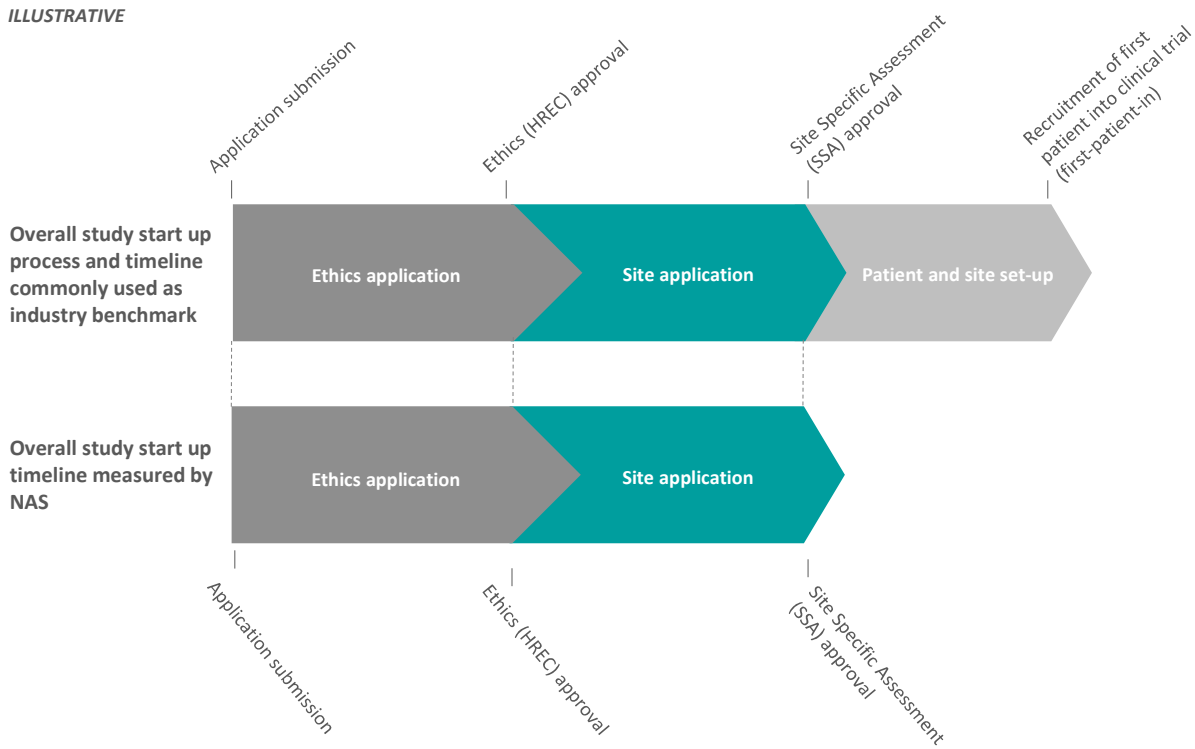
[33] Refer to Appendix E. ii Additional analysis outputs for more detail on growth by sponsor type

2.3.7 Clinical trial start up timelines

The NAS reports on the overall study start up timeline for Australian clinical trials. This period commences at ethics (HREC) submission and ends with the first SSA (Site Specific Assessment). This metric is designed to give:

- a real indication to sponsors of the time from submission of ethics application to possible site initiation and trial commencement; and
- an indication of the overall efficiency of the approval process for local policy stakeholders

Figure 12 Study start up timeline definitions[34]



According to the NAS, 19% of clinical trials in FY15 completed the regulatory process (ethics and site approval) in 60 days. Ethics approval appears to be slightly more efficient than site approval, with 88% of trials earning ethics approval within 120 days, compared to 79% completing site approval in the same amount of time.

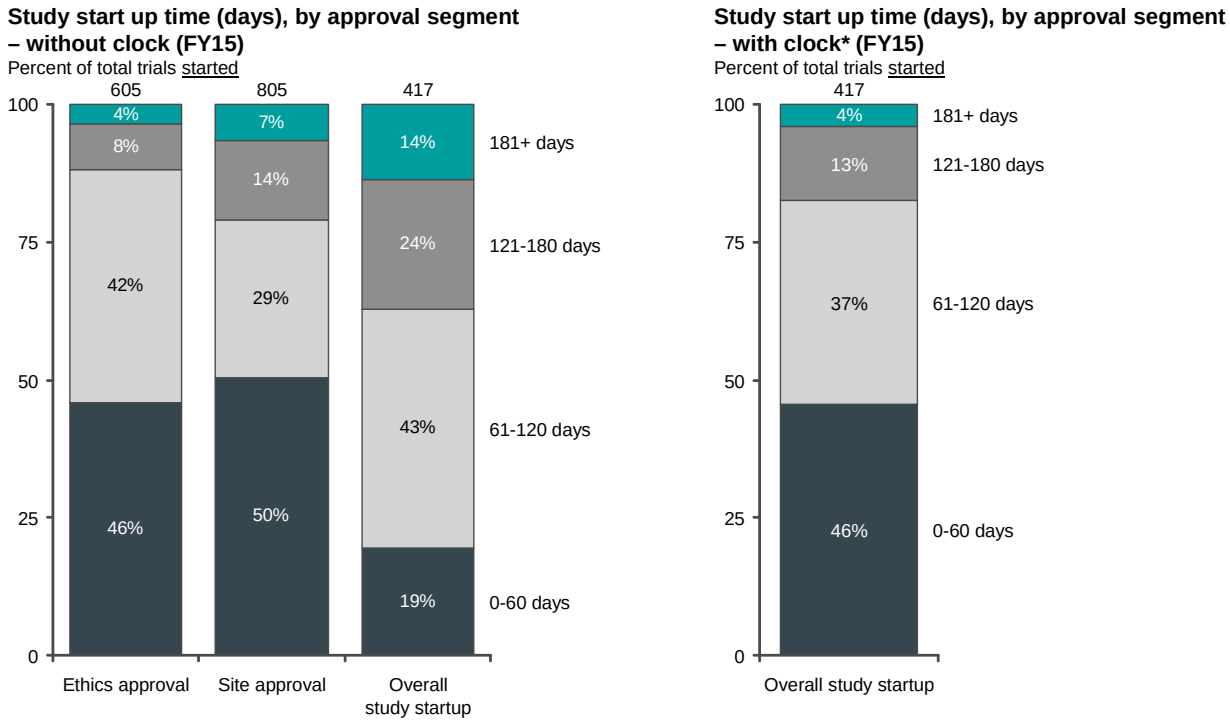
A more common start up efficiency metric or benchmark internationally is the time from the initial application to the point of first patient recruitment into a trial ('first-patient-in'). The NAS does not currently track the time between regulatory approval (including ethics and site

[34] Length of each chevron is not indicative of timelines. Diagram is illustrative

approval) and first patient recruitment, and therefore international comparisons to the NAS cannot be made on a like for like basis.

The NAS measures start up time with and without an administrative clock. The administrative clock is used specifically to measure the timelines of ethics administration, and it deducts the amount of time that the ethics or SSA application is with the investigator, trial coordinator, sponsor or CRO, to give a true measure of the time applications sit with government agencies. When the administrative clock is utilised for ethics approvals, the percentage of trials meeting a 60 day timeline increases from 19% to 46%. This increase suggests that there may be an efficiency lag created by communication and document iterations between investigators / trial coordinators / sponsors / CROs and ethics committees or research governance officers.

Figure 13 Clinical trial start up times, by approval segment



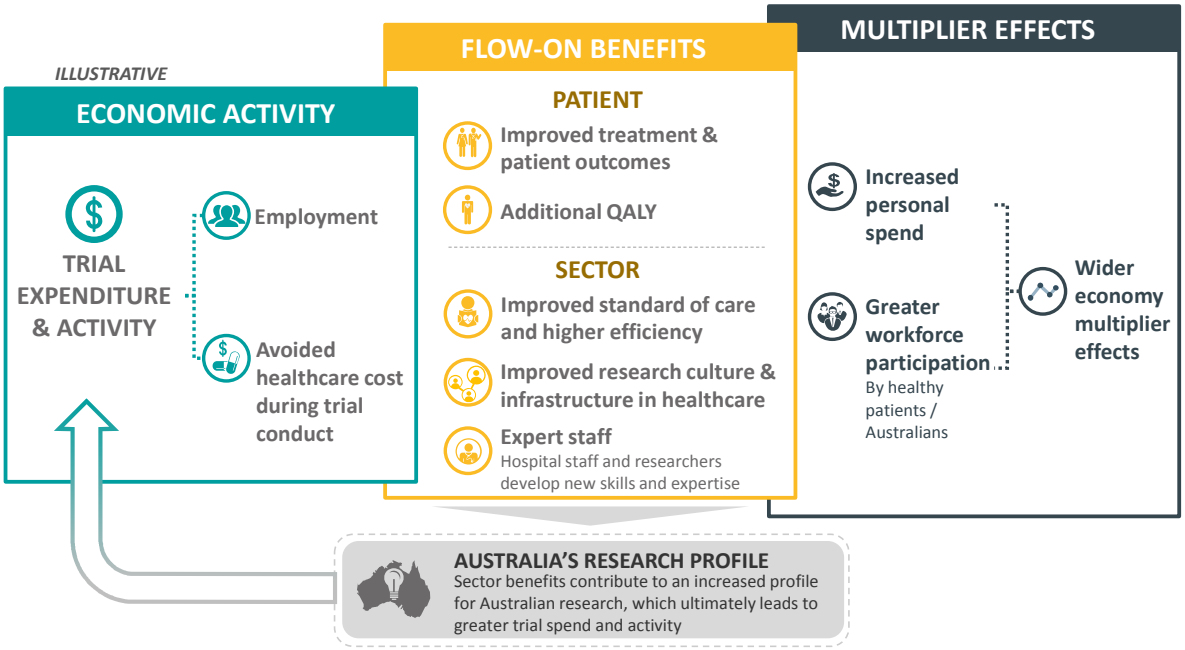
Note: * 'with clock' measures the time intervals between request and receipt of further information from investigator / trial coordinator, sponsor / CRO and this interval is deducted from ethics approval timing only. Data has not yet been collected for site assessment with clock
Source: NAS; L.E.K. analysis

3 The value derived from clinical trials in Australia

3.1 Overview of value derived from clinical trials activity

The clinical trial activity that is observed in Australia is supported by considerable direct investment and delivers a broad range of benefits for the economy and the wider society. A framework summarising these benefits is outlined in Figure 14.

Figure 14 The value of clinical trials in Australia



Clinical trial **economic activity** includes investment (trial expenditure), jobs and avoided cost to the healthcare system during the trial that would have otherwise treated trial participants.[35] This activity leads to a range of **flow-on benefits** from conducting trials both for patients through early access to new treatments and improving care outcomes, and for the sector through a strong research culture, improved standards of care, and a highly skilled workforce. For the wider economy, clinical trial activity results in **multiplier effects**, including increased personal spend by healthier participants and people employed in the jobs supported by the sector, and greater workforce participation (and hence economic contributions and tax revenue) by those patients who are healthier as a result of trial activity. However, clinical trials that extend life expectancy can also lead to greater costs to the health care system over time for certain types of participants.

The development of a thriving and innovative research culture within Australia's healthcare system leads to an improved international research profile for Australia and a stronger

[35] For industry sponsored trials, the treatment costs of participants enrolled in the trial are typically borne by the trial sponsor

understanding of the cost-effectiveness, safety and efficacy of treatments in the context of the Australian health system. Local clinical trial activity also supports and encourages the development of local MTP companies. In turn, this contributes to attracting more expenditure and researchers to Australia, increasing clinical trial activity (both local and global) and compounding the quantum of benefits in the sector, the economy and the wider society.

The sections below describe each of these benefit categories in more detail, and provide a quantification of the economic activity of the clinical trials sector in Australia. The quantification of the flow-on benefits and multiplier effects is outside the scope of this report.[36]

3.2 Economic activity

3.2.1 Clinical trials expenditure and funding

It is estimated that the clinical trials sector contributed **approximately $1.1 billion** in 2015 to the Australian economy as direct expenditure or investment.[37] For comparison, the OECD estimates that Australian expenditure on health and medical research & development (R&D) was approximately $4.3 billion in 2008 (the most recent year data was available).[38] This figure of $1.1 billion represents the direct expenditure to conduct clinical trials and excludes any expenditure on support infrastructure or overheads (e.g. large scale or capital intensive equipment, specialised environments or trial network support services). This figure also does not consider the economic value of flow-on benefits or multiplier effects. It consists of investment by MTP companies ($930 million), grants from the National Health and Medical Research Council (NHMRC, $100 million) and a range of other funding sources ($64 million), including state government funding and philanthropy. However, it must be noted that industry investment, and a portion of expenditure from other private sources, may be eligible for 38.5% to 43.5% reimbursement from the government through the R&D tax incentive.[39]

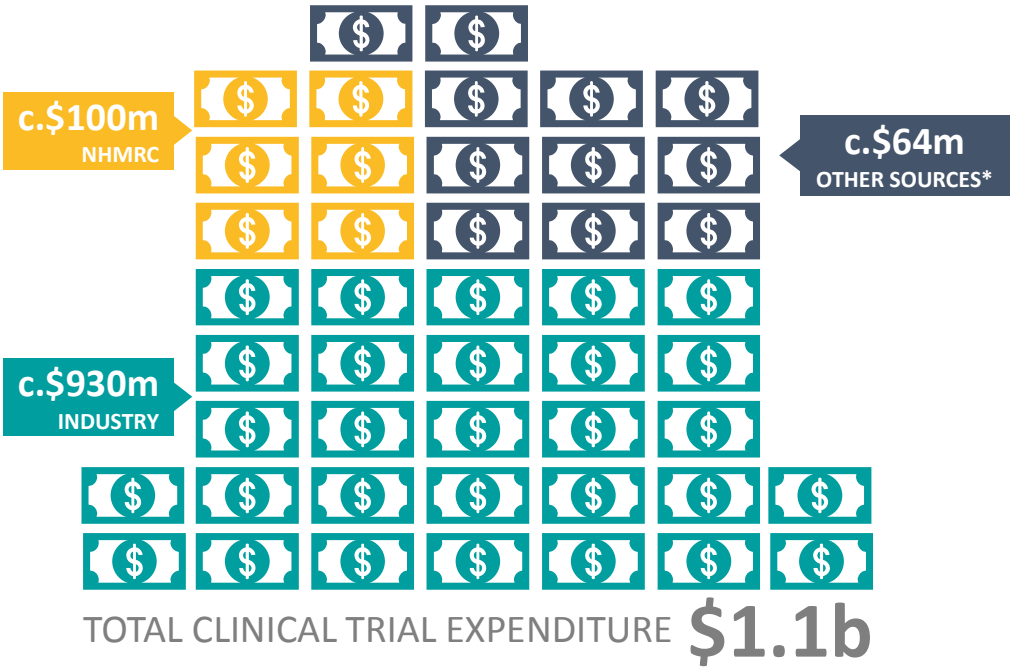
[36] For a recent review of the benefits from implementing a subset of trials in the Australian healthcare system refer to ACTA, Economic evaluation of investigator-initiated clinical trials conducted by networks, 2017 (based on an analysis of 25 high impact clinical trials)

[37] Detailed calculations are provided in Appendix G. - i. Trial expenditure / funding

[38] OECD stats data; Gross domestic expenditure; Includes business, government, higher education and private non-profit expenditure on Medical and Health Science R&D

[39] ATO identifies two incentives: a 43.5% refundable tax offset for eligible entities with an aggregated turnover of less than $20m p.a. or a 38.5% non-refundable tax offset for all other eligible entities

Figure 15 Total clinical trial expenditure in Australia[40]



Note: * Other sources is estimated based on funding flowing through MRIs and Clinical Trial Networks and includes funding originating from other government bodies (primarily state governments), philanthropic donations, and a range of other sources

Industry expenditure is based on clinical trials expenditure by MTP companies and CROs. The estimate of approximately $930 million is based on findings published in the Pharmaceuticals Industry Council (PIC) report in 2011.[41] In developing the report, the PIC surveyed major pharmaceutical, medical device and biotechnology companies, as well as CROs, to determine their annual expenditure on clinical trials in Australia.[42]

This industry expenditure pays for, or supports, a range of services and products within the clinical trial sector including:

- trial staff within MTP companies and CROs – staff dedicated to the non-clinical management of trials
- clinical and non-clinical staff within hospitals and trial sites – staff who are involved with both industry sponsored and non-industry sponsored trials

[40] Funding from other sources was estimated by analysing non-NHMRC and non-industry funding flowing through MRIs and Clinical Trial Networks. See Appendix G for calculation details. The estimate of clinical trials expenditure at MRIs is likely understated as funding can bypass MRIs and flow directly to partnering institutions such as universities or hospitals. Calculations are based on Association of Australian Medical Research Institutes (AAMRI) figures only. Additionally, ACTA's 'Profiling Networks Report' suggest that universities, networks and MRIs may supplement funding with their own sources, to support the clinical trials they administer. Supplementary funding includes in-kind value added to grants received. The value of this supplementary funding has not been estimated or included

[41] Pharmaceuticals Industry Council, 2011 Survey of Privately Funded Clinical Research Activity, 2012. The PIC has since been disbanded and is no longer collecting data within the sector

[42] This method may have led to an overstated figure as the underlying survey included both MTP companies and CROs. Some spend reported by CROs may have already been spent by MTP companies

- drugs, treatments and diagnostic tests – in the investigative and in some instances also in the control arms of trials. Industry may also fund the investigative therapies post-trial until they are approved in Australia
- patient costs (e.g. transport, non-drug pharmacy costs)

The NHMRC is currently the largest single source of direct government funding for IITs or non-industry sponsored clinical trials in Australia. The NHMRC estimates that approximately $100 million flows to clinical trials annually through a range of programs including projects, fellowships and scholarships, which represents approximately 9% of total expenditure on clinical trials in Australia.[43] In 2016, project grants alone provided $66 million of dedicated funding to Australian clinical trials.[44]

The majority of NHMRC funds are provided to universities, MRIs and investigators (individual or within a Clinical Trials Network) to conduct a range of investigational trials and observational studies. NHMRC grants are typically allocated to projects or studies that fall within the National Health Priorities defined by the Federal Government.

Other sources of clinical trials expenditure include other government expenditure (e.g. by state governments), overseas grants, charitable donations, academic institutions and self-funded investigators or institutions. Data on the amount of funding from these sources are generally not collected and reported in aggregate due to the fragmented nature of funders and recipients. Instead, the quantum of these sources was estimated by considering them collectively as funding received (and hence spent) by MRIs and other institutions or distributed through Clinical Trials Networks.

Clinical Trial Networks are used as a conduit for funding to MRIs, universities and other coordination units. However, Clinical Trial Networks do not directly provide funding themselves. Based on ACTA funding reported to flow through Clinical Trials Networks, it is estimated that in 2015 approximately $12 million was spent on IITs which involved Clinical Trials Networks and their associated institutions of hospitals and universities. This excludes any funding that they have received from NHMRC grants and industry sponsorship.[45,46]

Excluding funding received from NHMRC and revenue from the provision of commercial research services, it is estimated that MRIs received and spent at least approximately $53 million on clinical trials in 2015.[47] This expenditure is lower than for other market participants, as many MRIs focus on earlier stage research and about half of all registered trials are non-drug trials and are likely procedural-based trials or observational studies which are expected to have a lower total cost.[48,49] Funding to MRIs and through Clinical Trial Networks has some degree of

[43] L.E.K. / MTPConnect interviews and correspondence with NHMRC, 2017
[44] NHMRC - special data extract provided by NHMRC in 2017; NHMRC Research Funding Data - 2000 to 2015
[45] ACTA, Report on the Activities & Achievements of Clinical Trials Networks in Australia 2004-2014, 2015
[46] Further details are provided in Appendix G. - i. Trial expenditure / funding
[47] Based on AAMRI figures only
[48] Based on analysis of ANZCTR dataset.
[49] The estimate of clinical trials expenditure at MRIs is likely understated as funding can bypass MRIs and flow directly to partnering institutions such as universities or hospitals. Calculations are based on AAMRI figures only

overlap due to the involvement of some MRIs within Clinical Trials Networks. It has not been possible to determine how much these funding figures overlap or double count.

While the total estimated annual expenditure of $1.1 billion is expected to represent the majority of funding within the sector, it is acknowledged that some expenditure has not been captured such as:

- funding for IITs at hospitals, academic institutions and other types of medical treatment locations (e.g. General Practitioner offices) that are not associated with Clinical Trials Networks or MRIs
- funding for clinical trial infrastructure support, e.g. large equipment such as imaging machines

Changes to the level of total expenditure across time will come from underlying market dynamics. In addition the expenditure total is expected to shift due to impending changes in government funding.

Through current initiatives under the National Innovation and Science Agenda, as well as future investment under the Medical Research Future Fund, the Australian Government is seeking to build Australia's capacity across the health and medical research pipeline from discovery to translation and commercialisation. As a part of the 2014-15 Federal Budget, the Australian Government announced the establishment of the MRFF, an ongoing source of funding for investment in medical research over the medium to long term. Under the Medical Research Future Fund Act 2015, the MRFF was established using the uncommitted balance of the Health and Hospitals Fund (HHF). This $1.0 billion investment grew to $4.6 billion through 2016, as savings from the Health portfolio and residual amounts from the HHF were added. Further credits to the account are expected to consist of Health portfolio savings, until the capital value reaches $20 billion. The MRFF is expected to reach a balance of $20 billion in 2020-21.[50]

The net earnings from the MRFF are to serve as a permanent revenue stream, with disbursements of $1.4 billion expected over the next five years from 2016-17. This would effectively double the Australian Government's direct investment in health and medical research and innovation. The MRFF's first disbursements of $65.9 million have been announced and includes $33 million for clinical trials "to build on Australia's world class strengths and to ensure Australia is a preferred destination for clinical trial research".[51] According to the Hon. Greg Hunt, the Minister for Health, the $33 million investment will be allocated to four key initiatives:

- $13m to support research into a number of public health areas which contribute to the highest burden of disease, including the application of precision medicine;
- $5m to ACTA to support their work in ensuring Australia maintains its world-leading clinical trial standards and continues to support the clinical trials sector;

[50] Australian Federal Budget 2017-18, Statement 7: Debt statement, Assets and Liabilities. Currently reporting $4.6b with interest

[51] Australian Federal Budget 2017-18, Health Portfolio Budget Statement

- $8m to support the next generation of Australian researchers – including a major boost to the number of National Health and Medical Research Council fellowship schemes;
- $7m to help redesign State and Territory clinical trial operating systems to support greater collaboration and help to establish a state-based, one-stop shop to centralise, streamline and rationalise clinical trial administration.[52]

As part of the National Innovation and Science Agenda, $500 million will also be invested in promising biomedical discoveries through the Biomedical Translation Fund (BTF). $250 million of Commonwealth funding over two years, matched by private investors, supports the BTF.[53] The BTF was created in 2016 and will complement the MRFF through the commercialisation of health and medical research. The first investments will come from OneVentures Healthcare Fund III and will provide $10 million to Prota Therapeutics to advance the development of a new treatment for peanut allergies in children.[54]

The overall outlook for clinical trials expenditure in Australia is further discussed in section 7.

3.2.2 Employment

The expenditure on clinical trials directly supports jobs in Australia as the majority of the cost of a trial is staff expenditure. Direct employment within the clinical trials sector is considered in two distinct segments:

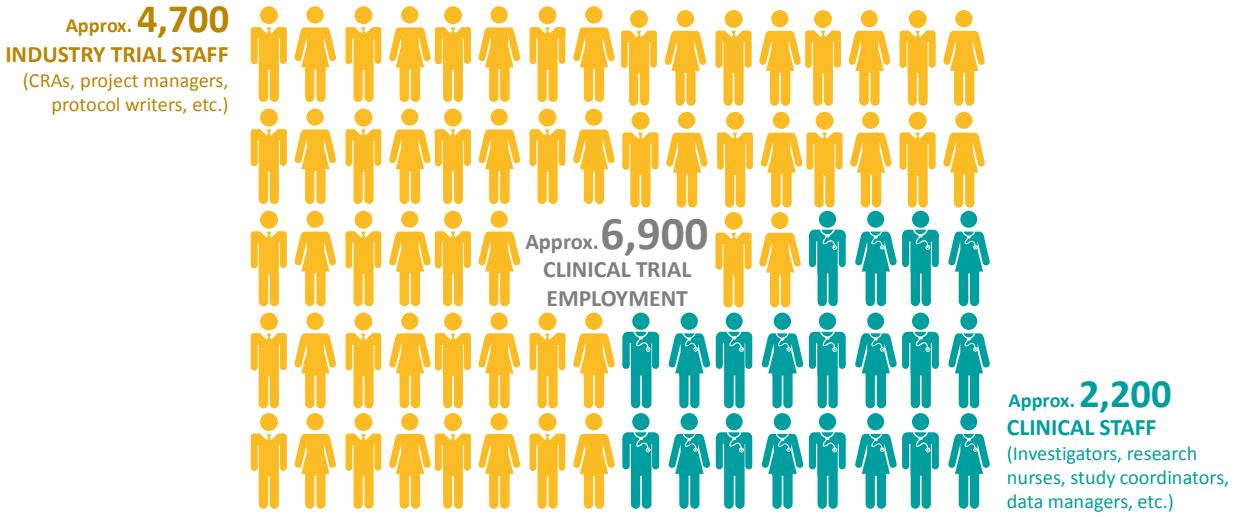
1. Clinical research and management staff employed at MTP companies, service providers such as CROs, MRIs and academic trial centres [55]
2. Clinical staff employed within hospitals, clinics or other trial sites

It is estimated that there were at least 6,900 jobs supported by the clinical trials sector in Australia in 2015.[56]

Staff employed within MTP companies and CROs are typically employed in direct clinical trial roles such as clinical research associates, medical or protocol writers, scientific advisors, project managers and oversight, regulatory, safety and quality officers and staff focused on data analysis such as data managers, biostatisticians, and statistical programmers. It is estimated that there were approximately **4,700** jobs supported within MTP companies and CROs in Australia for the management of clinical trials in 2015 (excluding those in MRIs or academic trial centres).[57]

[52] Media release by the Hon. Greg Hunt, "Delivering $33 million to help fund our next medical breakthrough" (19/05/2017)
[53] Department of Health Fact Sheet
[54] Media release by the Hon. Greg Hunt and the Hon. Arthur Sinodinos AO, "First BTF investment aims to improve lives through innovation"
[55] At the time of preparation of this report, discrete quantitative data was not available for MRIs and academic trial centres
[56] 2015 numbers have been estimated based on 2009 survey results. Detailed methodologies and assumptions are provided in Appendix G. -ii. Employment
[57] Pharmaceuticals Industry Council, Assessing the Value of Industry Sponsored Clinical Trials, 2009. This figure has been scaled based on total trial volumes (ANZCTR) to obtain a 2015 figure. Detailed methodologies and assumptions on the manipulation of referenced statistics are provided in Appendix G. –ii Employment. Note that the PIC has since been disbanded and is no longer collecting data within the sector

Figure 16 Clinical trial employment in Australia



The conduct of clinical trials relies heavily on clinical staff at sites such as hospitals. These experts are either dedicated research staff hired specifically for a trial or are regular clinical staff with trial training that have part of their time funded and allocated to trial activity. These roles typically include the investigator and co-investigator, study coordinators, research nurses, administration staff and data managers.

Using the results of a survey of 175 investigators and study coordinators conducted by the Pharmaceutical Industry Council (PIC), it is estimated that there were approximately **2,200** clinical staff supported by the conduct of clinical trials in 2015.[58] Given this data was collected through a survey that was not all encompassing, this number is likely underestimated and does also not include ancillary clinical staff such as diagnostic technicians and overhead / support roles.

Though many of these staff are salaried employees within the healthcare system, many of the positions are financially supported by industry. A study of clinical research sites conducted by the Pharmaceuticals Industry Council R&D Taskforce found that approximately 14% of investigator roles and 75% of support roles such as study coordinators are funded from fees earned via industry funded research.[59] Without the industry activity and inbound investment, many of these jobs would not exist and the capacity for investigator initiated research within the healthcare system would be severely diminished. Industry stakeholders have observed a current shortage of both Clinical Research Associates (on the sponsor / trial management side) and Clinical Trial Coordinators (on the clinical / site side), creating challenges for the sector.

[58] Pharmaceuticals Industry Council, Assessing the Value of Industry Sponsored Clinical Trials, 2009 – numbers reported are headcount, not full-time equivalent (FTE), and may be double counted due to some survey respondents being employed within the same group (respondents provided details on employees in their group); Detailed methodologies and assumptions on the manipulation of referenced statistics are provided in Appendix G. -ii Employment

[59] Pharmaceuticals Industry Council, Assessing the Value of Industry Sponsored Clinical Trials, 2009

It is worth noting that the employment estimate in this report does not consider staff at universities and MRIs directly or indirectly involved in clinical trials in Australia, as these entities generally do not report their employment statistics in the required granularity.

3.2.3 Avoided healthcare and drug cost

Clinical trials, specifically industry sponsored trials, pay for treatment to participating patients on the experimental arm (and sometimes the comparator arm) during the trial as part of their overall clinical trial expenditure. This is considered a value add to the health care system, as these participants receive sponsored treatment that in many cases would have to be funded out of the existing health budgets and schemes. These costs include payment for pathology, pharmacy, imaging (e.g. x-ray, magnetic resonance imaging), lab tests and drug costs that essentially cross-subsidise hospital costs for treating such patients.

3.3 Flow-on benefits

3.3.1 Sector benefits

Through funding clinical trials, the sector generates a range of broader benefits. Clinical trials produce results, in the form of new, proven treatments or improvements to standards of care, that deliver long-running benefits when implemented in the Australian healthcare system. Some trials (e.g. IITs) that are not motivated by commercial imperatives aim to determine the most cost-effective treatment from a range of existing options. The outcomes of these trials can result in changes to standard of care treatments that can bring ongoing financial savings to the wider healthcare sector.

Clinical trial funding and conduct also result in the enhancement of health system capacity and capabilities. It allows the training of research support (e.g. CRAs) and clinical research employees (e.g. investigators, study nurses), leading to an increase in human capital in the sector. Krzyzanowska, Kaplan and Sullivan (2011) state that clinicians and clinical research staff who participate in clinical research may have a better training and specialisation range that can be applied in research as well as standard medical practice.[60] Apart from being available as a highly skilled workforce to conduct trials, they are exposed to the frontline of clinical research and future standards of care (e.g. clinical trials raise awareness of the latest developments in clinical practice and support the uptake of new evidence-based findings into clinical practice in Australia).[61] This exposure may contribute to a faster application of the latest clinical knowledge in clinical practice, critical to ensuring the Australian health system is as efficient as possible in delivering optimal health outcomes in the population.

In addition to supporting capability and clinical practice development, the funding of trials also contributes to the availability of infrastructure at clinical sites (e.g. patient registries or biobanks / biorepositories). The availability of infrastructure and resource expertise translates into a wider value chain benefit that can support further R&D in the healthcare and MTP sector.

[60] M. K. Krzyzanowska, R. Kaplan, R. Sullivan; How may clinical research improve healthcare outcomes?. Ann Oncol 2011; 22 (Suppl_7): vii10-vii15

[61] Pharmaceuticals Industry Council, Assessing the Value of Industry Sponsored Clinical Trials, 2009

The sector benefits from clinical trials result in a symbiotic ecosystem that incorporates both industry sponsored trials and non-industry sponsored trials, where the activity of one segment is a critical benefit and building block for the other. On one side, industry sponsored trial activities and funding lead to the training of staff that can be leveraged for the conduct of non-industry sponsored trials. These spill over effects are critical for the existence of non-industry sponsored trials and their benefit to healthcare advances.

On the other side, IITs and high quality academic research build further capability and capacity, elevate care standards in Australia and contribute to raising the reputation of Australian medical experts, investigators and research staff at a global level, which in turn attracts more commercial funding and activity into the country. This self-perpetuating relationship is critical for Australia's trial activity, and the strength of both sub-sectors is essential in continuing to attract sponsors to conduct trials locally.

A healthy clinical trials ecosystem also contributes to enhancing the international reputation and links of Australian researchers. This enhances the ability of Australian medical experts to influence and gain experience in global medicine and device development (e.g. via participation in advisory boards or protocol writing). Trial activity and the attractiveness of the Australian research landscape from a global point of view also aids in retaining the top Australian medical experts and researchers within the health system.

In summary, the sector benefits underwrite an ecosystem that ultimately creates an elevated reputation of medical research and expertise in Australia. This contributes to the attraction of further trial activity and investment as long as the regulatory, cost and management conditions of trials are conducive as well. This implies a reinforcing cycle where economic and general sector benefits are compounded over time.

3.3.2 Participant / patient benefits

Clinical trials lead to benefits for patients directly participating in trials, patients treated in those hospitals that conduct trials and the wider society. Early access to new treatments or therapies at no cost is a key benefit for patients participating in clinical trials. This is particularly the case for patients that have already received standard treatments with unsuccessful outcomes, and who may benefit from new treatments that are otherwise not available in Australia. For example, an oncology patient may have exhausted all currently approved treatment options and be unable to work or enjoy a high quality of life due to the severity of their condition. This patient may then enrol in a local clinical trial and receive treatment at no cost (to the patient), potentially leading to positive outcomes. As a result, the patient may return to health and re-join the workforce. Without access through the clinical trial, this same patient may have only accessed the treatment many years later once it was approved and listed on the pharmaceutical benefits scheme (PBS), foregoing economic contributions in the meantime and at which stage their condition may have progressed to a point where the treatment was no longer suitable.

A number of studies have also indicated that the broader patient pool in hospitals which are more actively engaged in research activities may demonstrate superior health outcomes that can be traced back to the training of staff and incorporation of new evidence into wider clinical

practice.[62] Clarke & Loudon (2011) argued that treatment in research settings may produce better outcomes, superior adherence to guidelines and better use of evidence. However, they also note the need for appropriately designed studies to substantiate the anecdotal evidence and magnitude of this effect. In general, this is also of relevance for IITs that lead to advances in clinical procedures and processes which may otherwise not be available.

Access to new treatments and improving patient care outcomes that flow from the conduct of clinical trials can ultimately lead to superior health outcomes and health-related quality of life (HRQoL) across the aggregate of clinical trials and participating institutions. Johnston et al (2006) investigated the health outcome impact across a sample of 28 trials, demonstrating that the program of trials generated significant additional quality-adjusted life years (QALY) across participants and society.

3.4 Multiplier effects

The economic activity and flow-on benefits generate broader benefits throughout the economy, often referred to as multiplier effects. These include the economic effects of the 6,900 people employed in the clinical trials sector. By supporting professional, well-paid jobs in Australia the clinical trials sector creates economic multiplier effects as these employees spend their salaries in the local economy. This effect is further accentuated by the fact that much of the investment in clinical trials that supports these jobs originates overseas. Without this investment in trials, these jobs would not exist in Australia.

Improved treatments and standards of care that result from clinical trials, and the associated increase in QALYs, also contribute to a general population that can work longer and contribute more to the economy through production of goods and services, disposable income and spend, as well as taxation. However, clinical trials that extend life expectancy can also lead to greater costs to the health care system over time for certain types of participants. A quantitative estimation of these impacts remains inherently difficult although a number of studies have attempted to estimate the quantitative impact on a limited scope.[63]

Considered on a cost effectiveness / return-on-investment basis, clinical trials are believed to add additional years to the productive lifespan of citizens at a much lower cost compared to the value of the per-capita GDP output of that citizen (i.e. the return-on-investment is high).[64]

[62] M. K. Krzyzanowska, R. Kaplan, R. Sullivan; How may clinical research improve healthcare outcomes?. Ann Oncol 2011; 22 (Suppl_7): vii10-vii15; W. Van Gijn, P. Krijnen, V.E.P.P. Lemmens, M. Den Dulk, H. Putter, et al.. Quality assurance in rectal cancer treatment in the Netherlands: a catch up compared to colon cancer treatment. EJSO - European Journal of Surgical Oncology, WB Saunders, 2010, 36 (4), pp.340; Bois, A. D., Rochon, J., Lamparter, C. and for the AGO Organkommission OVAR PFisterer, J. (2005), Pattern of care and impact of participation in clinical studies on the outcome in ovarian cancer. International Journal of Gynecological Cancer, 15: 183–191; Majumdar SR, Roe MT, Peterson ED, et al. Better outcomes for patients treated at hospitals that participate in clinical trials, Arch Intern Med , 2008, vol. 168 6 (pg. 657-662)

[63] ACTA, Economic evaluation of investigator-initiated clinical trials conducted by networks, 2017 (based on an analysis of 25 high impact clinical trials)

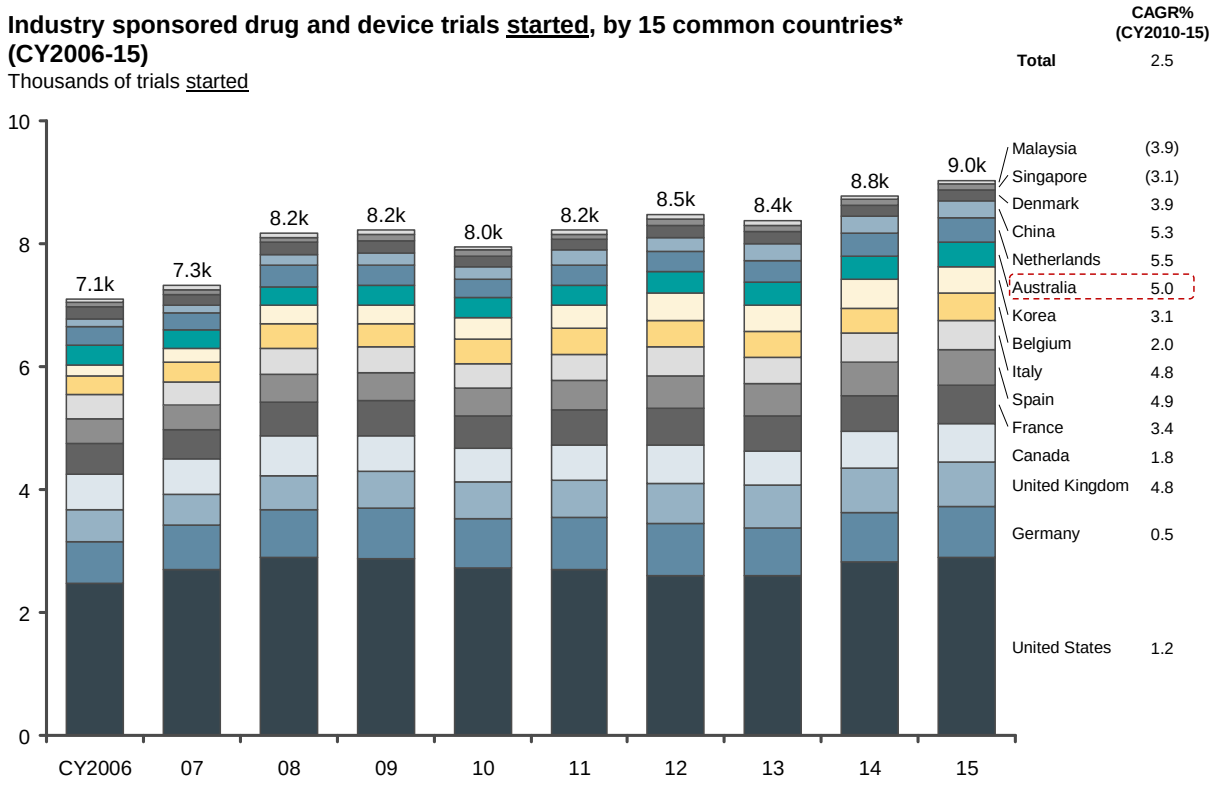
[64] Johnston, S Claiborne et al., Effect of a US National Institutes of Health programme of clinical trials on public health and costs, The Lancet , Volume 367 , Issue 9519 , 1319 - 1327

4 Australia's position and competitive advantage in the global marketplace

Clinical trials activity is a growth sector in many countries around the world and is driven by a country's desire to improve access to innovative healthcare as well as fostering a thriving local R&D and life sciences sector. The clinical trial activity and the benefits described in the sections above are heavily linked to Australia's position in this global marketplace. This is relevant for all types of trials in Australia but particularly industry sponsored drug and device trials, as local entities and sites compete for allocation and funding with other markets.

Australia has experienced strong growth in trial commencements in the period since 2010. In comparison to the countries with the highest trial activity, as well as a set of regional competitors, Australia has demonstrated higher growth rates than most countries in this competitor set (Figure 17).

Figure 17 Industry sponsored drug and device trials, by country



Note: * Common countries includes the top 13 countries by trial starts in 2015 plus Singapore and Malaysia. Excludes 'Withdrawn' trials. Trial counts are based on planned recruitment within each country – the same trial may be counted in multiple countries
Source: ClinicalTrials.gov (as at 06/02/2017); L.E.K. analysis

While the underlying analysis is limited by how comprehensively ClinicalTrials.gov tracks activity across countries, it can be regarded as directionally correct.

To understand the particulars of Australia's position in the global context and what brings investment, or keeps investment from coming into Australia, it is critical to assess factors driving

choice of geography for clinical trials as well as the drivers of and impediments to competitive advantage relative to other markets.

For the purpose of this report, the drivers and impediments / threats to Australia's position globally have been identified from interviews with global and local decision makers and those involved in clinical operations management, along with a review of recent sector reports such as the Federal Department of Health's *"Analysis of Recently Conducted Clinical Trials".* [65]

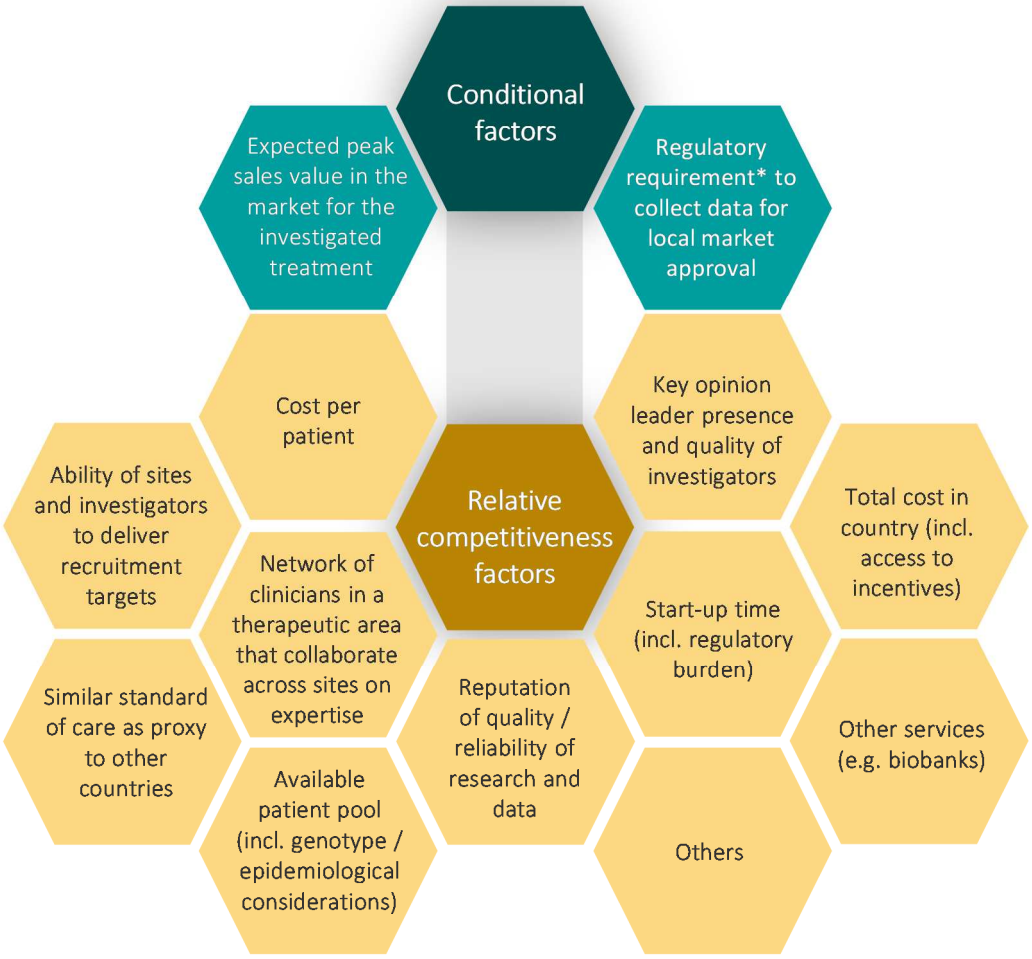
4.1 Factors driving choice of geography and competitive advantage

For the large subset of trials that are industry sponsored or industry funded IITs, Australia competes in a regional and global market. Figure 18 depicts a range of factors that drive sponsors to make choices on countries for trial site destinations, which can be broadly classified into two categories:

- **conditional factors**. These include commercial factors such as the expected peak sales value in the market of the therapeutic strategy under investigation. It also includes regulatory factors such as the requirement of local trial data collection for registration. The presence of these criteria may mean that a country must be included in a trial plan, irrespective of how competitive it may be. Lack of availability of required patient population (e.g. genotypes) can also act as a pre-condition, ruling out a country if required genotypes are not available or plentiful. These factors however are not the main determinant of trial scale in a country, which is mainly based on the competitiveness of the trial destination (see below).
- **relative competitiveness factors.** This range of factors, with varying degrees of importance, determine the competitiveness of a country to deliver on the objectives of the trials, and tend to be the most influential in the decision making process. They form the components of a rigorous comparative assessment between countries to determine if a country becomes part of a trial (i.e. in absence of conditional factors to consider) and the scale of the trial activity in a country (e.g. number of sites and participants). The range and weight of these factors may differ by trial and sponsor type. For example, while cost may be of lower importance for multinational pharmaceutical companies, it is a critical factor for smaller and medium sized entities and for medical technology companies.

[65] Australian Government Department of Health, Analysis of Recently Conducted Clinical Trials, 2015

Figure 18 Factors considered in the choice of trial geography



Note: * Regulatory approval in country regardless of planned sales channel

4.2 Drivers of competitive advantage in Australia

Market participants recognise a number of drivers that support Australia's competitiveness in comparison to other markets in attracting investment and clinical trial activity. While there are differences at the level of therapeutic area (TA) and trial type, the main drivers of Australia's competitive position are considered to include quality research and medical staff, quality of data and research output, the CTN / CTX scheme and efficient ethics approvals (which can help support rapid trial start up), specialised infrastructure and R&D tax incentives.

Table 5 Drivers of Australia's competitive advantage[66]

Competitive driver	Description	Resulting advantage
Medical experts of global standing and research staff	• Australia has a good reputation for the quality and global standing of its investigators and the networks between them. Health and medicine is one of Australia's strongest fields of research and Australia ranks highly against a range of international benchmarks. For example, medical experts (i.e. Key Opinion Leaders [KOLs]) are considered to be one of the biggest drivers of Australia's comparative advantage in oncology and their involvement with global sponsors contributes to driving trial activity in Australia. Perceptions of safety are also key enablers to recruitment and retention in Australian clinical trials[67]	**Internationally recognised, respected and accepted research output**
Quality of research & data	• Australia has an excellent reputation in science and research that is supported by quality publications. Compliance with Good Clinical Practice (GCP) guidelines and general high standards result in high quality data from Australian trials • Data collected in Australian trials is also accepted by a number of international regulators including the FDA and EMA	
TGA CTN / CTX and ethics approval	• The convenience and speed of the TGA notification scheme is consistently mentioned as an advantage relative to other markets • After significant reform efforts, the ethics process is also considered very competitive in Australia, particularly for trials at private sites or high volume sites (e.g. oncology)	**Fast and efficient trial environment** (especially for Phase I, oncology and private sites)
Specialised and dedicated infrastructure	• Australia's Phase I specialised service providers and sites are highly regarded in terms of quality and speed of delivery supported by streamlined processes and private ethics committees. Small and medium sized entities in the Asia Pacific region value these benefits highly and consider Australia as a bridgehead into other advanced health system countries • Sites with dedicated clinical trial offices and staff are significantly more effective in recruiting patients and delivering high quality data	
R&D tax incentives	• Commercial trial sponsors consider the availability of the R&D tax incentive that provides tax relief for eligible R&D activities as a key driver of attracting trials to Australia. This is particularly a factor for smaller and medium sized entities and their early phase studies • However, an R&D tax incentive review report was released for public consultation in 2016 with the goal of improving the effectiveness and integrity of the program and which may limit the availability of the R&D tax incentive. The Federal Government is yet to formally respond to this report[68]	**Cost competitiveness**

The above findings are similar to the Department of Health's 2015 review of key drawcards to clinical trials in Australia in its "Analysis of Recently Conducted Clinical Trials" report.[69]

Apart from these key drivers there are other factors that are relevant but either less commonly considered or considered to be of lesser importance in supporting Australia's competitive advantage. These include: the diversity of the patient pool (i.e. patient genotypes), availability of value adding services such as biobanks / biorepositories, comparable and high standards of care that allow extrapolation of results, seasonal differences to major US and European markets

[66] Based on L.E.K. / MTPConnect interviews with sector participants

[67] Federal Department of Health (on behalf of the CTJWG), Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials, 2016

[68] The Federal Government has not responded as of the release of the 2017-18 Federal Budget

[69] The report identifies the CTN/CTX scheme, R&D tax incentive, good reputation of dedicated research teams and key opinion leaders, and the willingness of the population to be involved in research as key drawcards for the conduct of clinical trials in Australia. However, the Department of Health acknowledges that several recent case studies indicate a lack of awareness or willingness to participate in clinical trials by the medical community and Australian public. Based on this feedback, and sector interviews, MTPConnect believes that patient recruitment is more a barrier than an asset to success at this time

(e.g. for trialling of flu vaccines), the English language, and an established and mature reimbursement framework. Australia also has comparable variable costs (labour and treatments) to other developed markets (at long run exchange rate averages), and some fixed costs are even lower thanks to efficient processes such as the CTN system. However, this advantage can be eroded due to lower patient recruitment rates, delays in site governance, and a lack of consistent costing, which can result in higher per patient costs (as explained below).

4.3 Impediments and threats to competitive advantage

While there are strong rationales driving Australia's competitive advantage and selection as a trial location, market participants also consistently report a number of factors that either prevent Australia from being considered as a destination, or that impact the conduct and success of the trial. These factors are impediments and threats to competitive advantage and inbound investment, specifically as other markets in the region (e.g. China, Taiwan and South Korea) and other emerging markets (e.g. Eastern Europe, Latin America) provide key advantages such as size of patient population and continue to improve their processes. While these countries have obvious advantages in population volume, they often do not exhibit the population diversity and high quality that is central to Australia's strengths.

Table 6 Barriers to Australia's competitive advantage[70]

Impediment Driver	Description	Resulting Barrier
Governance approval process	• Despite improvements to ethics approvals, the site governance approval process is often lengthy and highly variable from site to site and study to study • This reportedly erodes some of the advantage achieved in the ethics and notification process, putting start up times at risk in comparison to other markets and reducing local recruitment time windows • Low performing trial sites may be removed from selection for future trials by sponsors or service providers, reducing the opportunity for local research spill over effects and limiting the total potential patient pool • Lengthy start up times has an effect on all sponsors but is particularly relevant as a decision making factor for global trials and for medical technology studies, given shorter product lifecycles	Variability in start up time
Patient recruitment and economics	• Australia's small population size relative to other markets such as the UK, US, Eastern Europe and Asia creates a barrier to high patient recruitment levels. In addition to this (and relative to countries with a similar population such as Canada) the average number of participants per trial site in Australia is generally lower • This is compounded by a general lack of effectiveness in referrals between sites and other healthcare entities. This is particularly evident considering Australia's well developed health system, where a number of diseases are routinely managed in the primary care setting (GPs). These lack recruitment data linkages to local clinical trial sites, which in Australia have been predominantly located in large, tertiary hospitals • 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	High per patient costs

[70] Based on L.E.K. / MTPConnect interviews with sector participants

Capabilities and capacity in early stage high risk and innovative trials (e.g. FTIH)	• Australia's ability to continue to attract a significant number of early phase trials requires further investment in capabilities and capacity in more novel early stage trials (e.g. immunotherapy, First Time in Human [FTIH], biotechnology trials with focus on translational medicine) • Novel biologic therapeutics were identified as an area of particular attention, as FTIH trials tend to feature more emphasis on research work to prove the biological concept and integrate clinical pharmacology with translational research [71] • Experts believe that some Phase 1 sites in Australia lack the capability to effectively deliver these trials • If required capabilities are not available or sufficiently developed in the future, Australia may miss out on a growth segment of the sector	**Limited capabilities and bandwidth for high risk or innovative trials lead to difficulties in establishing a sustainable competitive advantage**

The above findings are similar to the Department of Health's 2015 "Analysis of Recently Conducted Clinical Trials" report, which reviews key barriers to the conduct of clinical trials in Australia.[72] Market participants and the Department of Health report also referred to other factors, such as costs, that are having an adverse impact on Australia's outlook as a trial destination. While the cost to conduct a trial in Australia is considered to be generally comparable to other mature markets, it does act as an impediment for some trials and / or sponsor segments that are cost conscious. For medical technology firms and small and medium sized companies, the cost to conduct a trial in Australia can be considered prohibitive when compared to regional alternatives. Cost of some trial sites can also be an impediment for large global pharmaceutical companies. However, a recent study identified that, for the majority of trials, cost was only a consideration of Australia as a trial location after capacity to recruit, timely trial start up, and experiences and highly qualified research teams.[73]

Consultations also indicate that Australia does not have sufficient animal testing facilities to meet the demands of pre-clinical research. Although pre-clinical research falls outside the definition of clinical trials, it is a crucial feeder for early stage clinical research. If local companies are forced offshore to conduct their pre-clinical research, Australia will be at risk of losing the resulting early stage clinical trials as well.

4.4 Australia's position and areas of strength in the global marketplace

These advantages and barriers directly influence the level of industry sponsored trial activity in Australia. To understand their effects it is helpful to compare Australia's trial activity and the focus areas within it against the global context. Australia's international position has a direct link to the level of investment that Australia can attract, which has direct implications on the entire sector, as industry sponsored activity has flow-on effects on non-industry sponsored studies by supporting clinical research skills and infrastructure.

This report compares Australia's activity to other markets based on information in the clinicaltrials.gov registry. Although this registry is US focused and does not capture all trials within individual countries, it is one of the most comprehensive global databases and thus most useful for comparing between countries on a like-for-like basis. The analysis is based on drug

[71] L.E.K. / MTPConnect interviews with sector participants, early 2017

[72] The report identifies cost, small population size, lengthy governance/ethics approval processes and poor research infrastructure and accountability as key barriers to the conduct of clinical trials in Australia

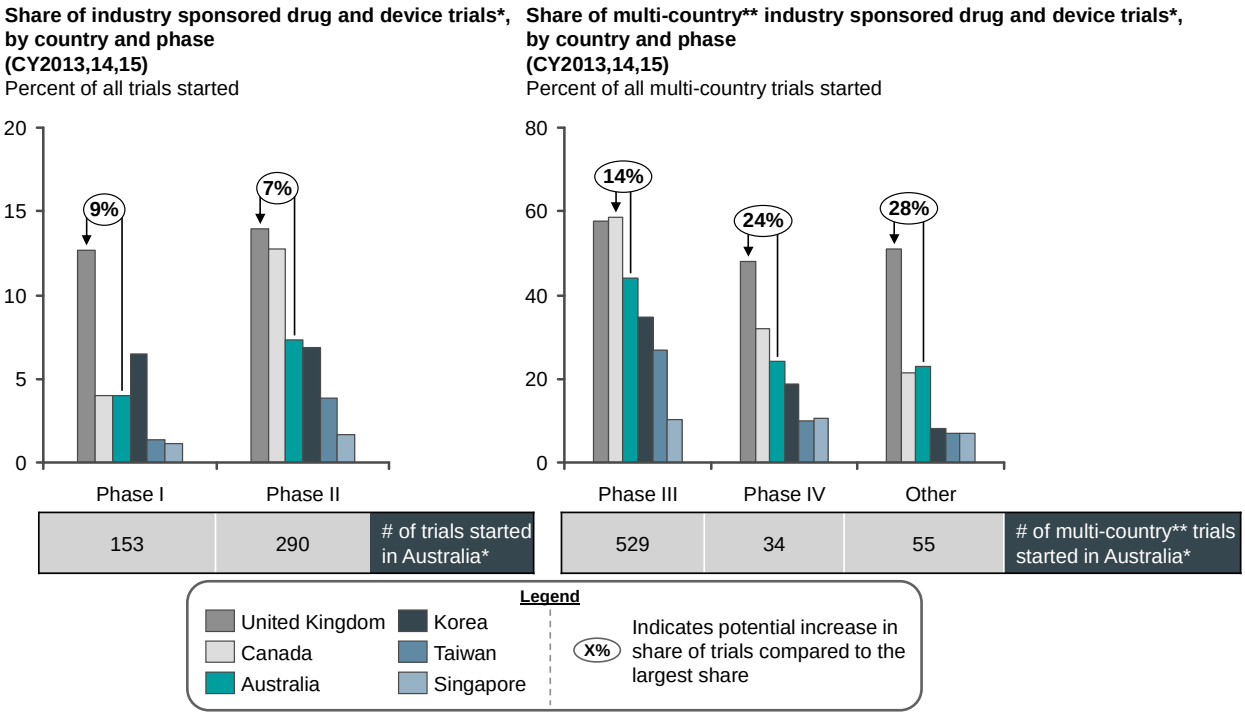
[73] Australian Government Department of Health - Analysis of Recently Conducted Clinical Trials, 2015

and device interventional trials by industry sponsors only as this sub-set is considered the most comparable across countries and most relevant to competitive advantage for commercial investment.[74]

In comparing Australia's mix of trials against countries with similar characteristics (e.g. Canada) and regional competitors (e.g. Singapore), noticeable differences emerge that describe Australia's domain, which are reflective of the drivers of Australia's competitive position.

Australia's performance across industry sponsored trials differs across the different stages (Phase I-IV – see Figure 19).

Figure 19 Industry sponsored trial starts, by country and phase



Note: * Includes Drug, Device, and Drug & Device intervention types only. Includes Industry and Industry & Other sponsored trials only. 'Withdrawn' trials are excluded; ** Multi-country trials defined as trials with enrolment in more than three countries
Source: ClinicalTrials.gov (as at 06/02/2017); L.E.K. analysis

In regards to Phase I trials, Australia seemingly exhibits a low market share (4%) of global industry sponsored trials relative to the UK (13%) but is on par with Canada. Australia's Phase I performance has to be assessed in contrast to the small size of its local MTP sector relative to other advanced markets, and also across time. Approximately 96% of the 153 Phase I trials in Australia are sponsored by offshore companies compared to only 66% of Phase I in the UK.[75] This shows that a considerable portion of the UK's Phase I trials are due to its larger local MTP sector, whereas Australia is attracting its Phase I trials from offshore companies. In recent years Australia has managed to attract an increasing number of FTIH Phase I trials and interviews with

[74] More than two thirds of Australia's activity is not registered in clinicaltrials.gov. These are mainly investigator-initiated trials that do not have a rationale for entry into the registry, or instead are entered into local registries such as ANZCTR
[75] Based on ClinicalTrials.gov analysis (as of 06/02/2017). Further details are provided in Appendix D.

sector participants suggest that the growth is mainly attributed to inbound activity from abroad and less sourced from local sponsors.[76] Between 2012 and 2015, Australia's growth in Phase I volume was 17.2% p.a. compared to 1.8% p.a. globally.[77]

Australia's advantage in Phase I trials is reflective of the competitive edge of specialised Phase I units. These Phase I units have a large number of staff, have quality management systems with standard operating procedures, can outsource to third party organisations instead of using hospital departments, and have IT infrastructure which enables better data tracking and quality assurance. They typically provide service 24 hours a day, 7 days a week, compared to public hospital sites that are often restricted to standard business hours. Phase I units conduct a large number of healthy volunteer studies and have access to databases with thousands of participants. With access to large patient pools and start up specialists to complete single centre research applications, start up times are much quicker at specialised units. Australia's Phase I units also benefit from a stable and streamlined regulatory environment that delivers leading start up times compared to other markets.

The CTN process for Phase I trials is expedited and offers flexibility relative to other markets such as the US and its Investigational New Drug (IND) application process via the US FDA. These benefits have been highlighted by the introduction of more restrictive regulatory developments in other markets (e.g. the EU clinical trials directive inhibits rapid FTIH Phase I start up in member countries that previously had an advantage such as the UK).[78] However, in April 2014, the EU approved regulatory changes to streamline application processes, more efficiently extend clinical trials throughout the EU, allow co-sponsorship and increase flexibility for low risk trials.[79]

The significance of this competitive advantage in Phase I trials is reinforced by the fact that the competitive impediments discussed at 4.3 are of relatively lower importance for Phase I trials. Variability in start up times due to governance process times is less of an issue in Phase I as the majority of the volume is passed through dedicated Phase I units with efficient ethics and governance approval processes. Further, patient recruitment and economics challenges are less prevalent due to lower participant number requirements for Phase I trials.

Across later stage trials such as Phase III trials, activity in Australia tends to be part of larger 'global' trials. Australian sites are included in approximately 45% of Phase III industry sponsored trials, 14 percentage-points behind Canada and the UK (see Figure 19). Interviews suggested Australia is part of a global 'circuit' of common host countries. Nonetheless, it exhibits a larger differential to other advanced markets such as the UK, which may be attributed to the UK's

[76] L.E.K. / MTPConnect interviews with local MTP sector experts

[77] Australia growth rate is for all Phase I trials, regardless of intervention type, and is derived from ANZCTR's combined dataset of ANZCTR & Clinicaltrials.gov for trials with recruitment in Australia (this growth may be a combination of actual growth but also increased registration compliance). Global growth rate derived from unique Phase I trials in Clinicaltrials.gov (as at 06/02/2017)

[78] EU Directive 2001/20/EC, implemented in 2004 in the UK. L.E.K. / MTPConnect interviews with local MTP sector experts

[79] EU Clinical Trials regulation (No 536/2014)

larger local industry sector, the size of its population or the competitive advantages of the UK trial sector respectively.[80]

Australia's share of Phase IV and 'Other' industry sponsored trials (including device trials) is lower, but typically on par with Canada. Canada is a particularly valuable point of reference for the Australian market, given its similar population and size. Canada's strong performance in global clinical trials may be attributed to its high recruitment rates (70% of the population report being interested in participating in clinical research) and a nationally coordinated approach to clinical trials.[81] Canada benefits from its close proximity to U.S. hubs and offers competitive R&D tax incentives. In Canada, corporations are eligible for a 15% investment tax credit on qualifying scientific research and experimental development spend.[82]

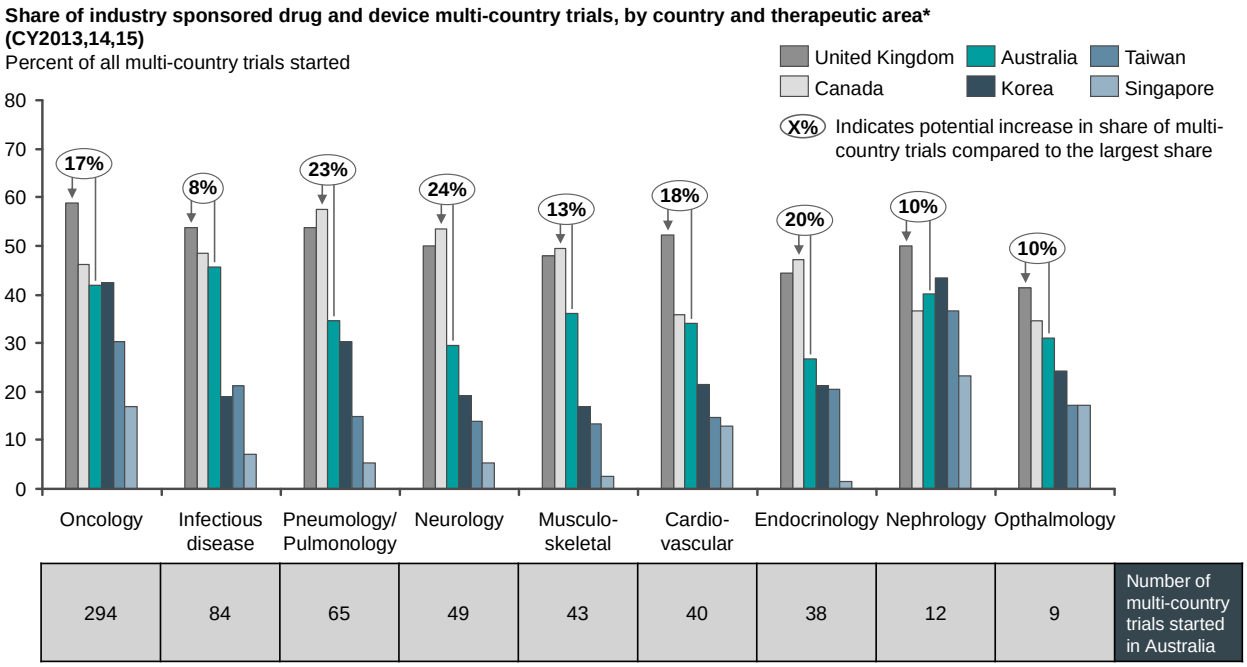
Interviews with industry participants suggest that there are two distinct segments of industry sponsored trials, each with different competitive dynamics:

1. Australia tends to have a stronger position in trials in complex or rapidly changing disease areas, or involving biological agents or trials with a complex design. These trials require high quality data and treatment environments, and high levels of KOL involvement especially in early stages. Australia has strong capabilities in these areas relative to emerging markets, and it tends to compete with North America and Western European countries in these trials.
2. Over the past five years, Australia has been increasingly competing with East Asia, Eastern Europe and South America in the conduct of trials:
    a. with lower design complexity;
    b. with lower requirements in capabilities, equipment and procedures;
    c. requiring large participant volumes;
    d. that are more exposed to cost per patient and recruitment barriers.

To illustrate this, Australia appears to perform better relative to advanced health system markets in oncology, infectious disease, musculoskeletal, nephrology and ophthalmology trials (see Figure 20). Australia's strength in the oncology sector for example is based on the reputation of Australian KOLs who are present on global advisory boards, superior specialised infrastructure and wider ranging networks compared to other TAs. In neurology on the other hand, Australia seems to be more challenged competitively but is believed to have a strong position in specific disease types such as Alzheimer's disease, due to the presence of globally renowned medical experts. Industry consultations also indicate that Australia has advantages in cardiac devices and neuromodulation.[83]

[80] L.E.K. / MTPConnect interviews with local MTP sector experts
[81] Canadian Clinical Trials Coordinating Centre "Clinical Trials – the Canadian Advantage" July 2016
[82] The Canada Revenue Agency indicates that a 35% investment tax credit is available to Canadian-controlled private corporations and a 15% rate is available to other corporations
[83] L.E.K. / MTPConnect interviews with sector participants, 2017

Figure 20 Individual country shares of multi-country trial starts, by therapeutic area (TA)



Note: ** Includes Drug, Device, and Drug & Device intervention types only. Includes Industry and Industry & Other sponsored trials only. 'Withdrawn' trials are excluded. Multi-country trials are defined as having planned recruitment in more than three countries. Therapeutic areas were determined using a search of key words within the 'conditions' field in the clinical trial database – excludes trials where multiple therapeutic areas were found

Source: ClinicalTrials.gov (as at 06/02/2017); L.E.K. analysis

TAs where Australia attracts fewer trials compared to other countries are generally those that are more strongly impacted by structural impediments to competitive advantage. According to industry experts, large scale trials (such as certain later stage trials in cardiovascular and metabolic disease) tend to bypass Australia as they have seen a trend towards being conducted with fewer sites but higher per-site patient numbers, which can be better served in large, densely populated countries.

Overall, Australia does show potential for competitive advantage given the right level of support and structural benefits in TAs or stages. In order for these advantages to be defensible and leveraged, Australia's sector stakeholders need to address evident threats and continue to support and invest into the identified sectors.

5 The policy stakeholder landscape and current state of reform initiatives

Australia's current strong competitive position and growth prospects in clinical trials are a product of a long history of active reform and improvements to how clinical trials are conducted. To further support the Australian clinical trial sector and address some of the impediments perceived from market participants, key sector stakeholders have worked to identify the priorities to improve Australia's international competitiveness as a destination of choice for clinical trials. Before giving an overview across these initiatives, this report outlines the stakeholder landscape that is driving this change.

5.1 Stakeholder & governance landscape

The Australian clinical trial stakeholder landscape is complex. Besides the market participants, it consists of multiple bodies that shape the sector's policy environment. This includes government agencies and government-affiliated bodies at state, territory and federal level, not-for-profit associations and health organisations. All stakeholders have different responsibilities, scope and roles, and can be considered on a spectrum from advisory to decision making bodies.

In addition to the policy landscape, multiple stakeholders are involved in the organisation and operational governance of clinical trials in Australia. Not all actions needed to drive improvements rest with governments. While sponsors, clinical investigators and the participants in their trials ultimately drive the conduct of clinical trials; health system managers, the biotechnology, pharmaceutical and medical technology industries are pivotal to advancing the sector. Achieving success requires a collaborative approach between all players.

Government involvement is multi-layered and crosses a number of portfolios. All state and territory Health Departments, the NHMRC, the Department of Health, TGA and DIIS, have been working together for a number of years to improve the clinical trial environment in Australia. As no single entity holds all levers for change in the sector, recent reform and major policy advisory efforts have been guided by three bodies to support a collaborative and partnership approach: The Clinical Trials Advisory Committee (CTAC), the Clinical Trials Jurisdictional Working Group (CTJWG) and the National Mutual Acceptance Jurisdictional Working Group (NMAJWG).

The **CTAC** was established to provide advice on the progress of remaining recommendations made by the Ministerial-appointed CTAG, as well as other activities to support the Australian clinical trial environment. CTAC includes representatives from all stakeholders in clinical trials, including the pharmaceutical industry (Medicines Australia), drug and biotech industry (Australia's Biotechnology Organisation [AusBiotech]), consumers (Consumer Health Forum), researchers (ACTA & the Australian Private Hospitals Association) and state and commonwealth governments and associated bodies (Department of Health, DIIS, TGA and the NHMRC).

In recognition of the important role that state and territory jurisdictions and hospitals have in progressing change in the clinical trials sector in Australia, the **CTJWG** was formed in 2014 following decisions made by the then Standing Council on Health. The purpose of the CTJWG is to identify and implement actions that will better enable a consistent national approach to

multi-jurisdictional clinical trials in Australia, and enhance Australia's ability to retain local trials and attract international trials. The CTJWG members are senior officials from the state and territory health departments and the NHMRC.

The **NMAJWG** was formed cooperatively by jurisdictions in 2013 and ultimately reports through the Australian Health Ministers' Advisory Council (AHMAC). It was created to oversee implementation of the NMA scheme for single ethics approvals and to advise the Hospitals Principal Committee (HPC) on all relevant matters.

As system managers, each jurisdiction is responsible for the overall management of health districts and / or public health organisations in its state or territory. This includes public hospitals, where most clinical trials in Australia are conducted. While governance arrangements within and between NMA jurisdictions have been agreed and are consistent, governance arrangements vary in other jurisdictions. Some states and territories operate in a fully devolved environment where responsibility for governance of public health organisations rests with health districts and / or public health organisations. Trial sites are ultimately responsible for the actual governance and conduct of clinical trials within their organisation.

The **TGA** provides a legislated regulatory framework for the availability of medicines, medical devices and biologicals within Australia. There are two TGA schemes under which clinical trials involving unapproved therapeutic goods may be conducted, the CTN Scheme and the CTX Scheme. The CTN scheme enables drugs and devices not registered on the Australian Register of Therapeutic Goods (ARTG) to be used in clinical trials, following notification to the TGA (use of notified products in a trial can only proceed following HREC and site-specific approvals for the trial). The TGA has made a number of recent improvements to CTN to support broader reforms, including the transition to an on-line submission and approval system (eCTN). The CTX scheme is a TGA approval process under which it assesses the evidence and approves the safety of proposed usage guidelines within individual trial protocols, prior to HREC and site specific approvals.

Among other focus areas, the **NHMRC** provides oversight and guidance frameworks for ethics review and approval across the country. The NHMRC has facilitated a number of ethics and governance policy changes in recent years.

In summary, the Australian policy stakeholder landscape is made up of a number of diverse bodies with different remits. Compared to other mature markets (e.g. the UK), the Australian Commonwealth does not have a single overarching clinical trials body that has national authority and oversight for governance formation, regulation enactment and ethics / governance approvals.

5.2 Current state of initiatives

A number of prior reports have identified the need to improve the competitiveness and timeliness of clinical trials in Australia, in order to attract more global investment. Most notably,

the Reports by the Pharmaceuticals Industry Strategy Group in 2008[84], the subsequent CTAG report in 2011[85] and the Federal Department of Health's recent study into patient recruitment and retention[86] outlined a large number of initiatives geared at improving the productivity, speed and cost of conducting clinical trials in Australia. The changes largely focused on:

- improving the speed of ethics and site approvals, including harmonisation across states
- standardising and reducing costs associated with clinical trials in Australia
- improving patient recruitment

In 2013, McKeon et al undertook a major review of health and medical research in Australia. The report, The Strategic Review of Health and Medical Research (the McKeon Review)[87], echoed many of the initiatives from the CTAG Report and called for better integration of clinical research capability within the health system. It also recommended replacing the numerous HRECs with 8-10 nationally based professionalised committees, implementing a national clinical trials liability scheme and establishing a national clinical trials office.

In addition to the CTAG and McKeon reports, the Federal Department of Health on behalf of the CTJWG has recently commissioned and released its "Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials". It recommended the establishment of dedicated structures at national and / or jurisdictional levels to improve leadership and coordination of clinical trials in Australia. This is consistent with collaborative work already underway within jurisdictions. Similarly, DIIS has established an interactive clinical trials web portal and framework for education and training governance, with the goal of expediting clinical trial reform in Australia.

All Ministers of Health and Industry & Innovation have acknowledged the importance of clinical trials in advancing clinical practice, health system sustainability and self-improvement, and stimulating the innovation economy. Efforts over the last decade to improve the clinical trials environment have resulted in incremental progress, however it is recognised that there is room for further improvement. In this context, in April 2016, the COAG Health Council tasked the CTJWG (via the AHMAC) with developing options to stimulate the clinical trials sector. CTJWG was charged with improving administrative efficiencies, better engaging sponsors and improving trial start up times and outcomes.

In accordance with this directive, jurisdictions have agreed to move forward with a focus on a refreshed approach to regional design and streamlined administration of clinical trial systems. In its March 2017 Communique, COAG reported "all governments have agreed to redesign trial operating systems around central coordinating units that will make it easier to conduct and participate in safe, high quality clinical trials. The Commonwealth has committed funding of $7 million over four years to support jurisdictional clinical reform."[88] This $7 million budget measure, titled Encouraging Clinical Trials in Australia, aims to establish state-based one-stop

[84] Pharmaceuticals Industry Strategy Group, Final Report, 2008
[85] Clinical Trials Action Group, Clinically Competitive: Boosting the Business of Clinical Trials in Australia, 2011
[86] Federal Department of Health (on behalf of the CTJWG), Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials, 2016
[87] McKeon et al, Strategic Review of Health and Medical Research in Australia, 2013
[88] COAG Health Council Communique (24 March 2017)

shops to streamline clinical trial administrative and operating systems in each state and territory. This reflects the current policy intention that national coordination is to be led by the CTJWG, achieved at a state level through a federated approach, and will not require a new governing body.

Other sector participants and reviews have also called for improved regulatory processes that employ a risk-based approach to regulation of clinical trials. This has largely been achieved within the sector through the introduction of the TGA's CTN / CTX scheme.

Beyond these overarching considerations and to achieve targeted sector reforms, a multitude of initiatives have been commenced or completed, involving a range of government and sector participants. A brief summary of these initiatives is provided below, with further details outlined in Appendix A.

Table 7 Summary of sector improvement initiatives

Initiative category	Key achievements	Major contributors	Status
Timeliness of ethics and research governance	• The TGAs CTN / CTX scheme for clinical trials involving unapproved drugs or devices	• Federal regulatory bodies and the TGA	• Implemented and highly effective
	• NMA scheme for single ethics approvals	• State / territory governments and public ethics committees	• Largely implemented with efficient ethics approval now common
	• Various improvements within state / territory health systems including efforts to enhance consistency of ethics and governance underway through the CTJWG	• State / territory governments (including via CTJWG)	• Implementation ongoing
	• Web based common ethics applications for human research (HREA) and national certification schemes for institutional ethics approval processes	• NHMRC, state governments, various ethics committees and trial sites	• Released on 14 December 2016. There are currently 4,000 registered users
	• Good practice process for streamlined site assessment and authorisation	• NHMRC	• Process was piloted at 16 sites throughout Australia. NHMRC is now working with nine sites on phase two of the process
Education and training	• A number of competency frameworks, e-learning modules and toolkits / training courses have been introduced to improve trial management skills in the sector	• NHMRC, ARCS, several state governments, PRAXIS and Swinburne University (commissioned by DIIS)	• Commenced and trialled but not well utilised
	• Coordinating Office in Victoria hosts targeted forums and workshops to inform the sector	• VIC government	• Ongoing since 2009
	• Conferences and seminars are hosted by industry associations to assist with the application of knowledge in the workplace	• ARCS	• Ongoing

Initiative category	Key achievements	Major contributors	Status
	• Competency frameworks and ethics-focused e-modules have been created for the HREC sector, with a specific emphasis on clinical trials	• PRAXIS	• Ongoing
Standard costs for clinical trial activities	• Standard table of costs for trials in Australia released in 2015	• IHPA	• Whole-of-sector uptake / use has not occurred. While market participants question if costs can be generalised across different trial types and sub-sectors, trial budgets remain a commercial negotiation process between sites and sponsors
Patient recruitment for clinical trials and e-health	• National clinical trials portal implemented (australianclinicaltrials.gov.au)	• DIIS and NHMRC	• Portal released with notification and subscription service added in 2015
	• E-health records in place but uptake has been slow, however this activity is part of a much broader reform agenda	• Australian Digital Health Agency and Dept. of Health	• E-health utilisation is poor / not targeted to trials
	• Increased patient education	• Cancer Australia, NHRMC, CTJWG & Health Forum	• Awareness campaigns are ongoing / to be launched
	• Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials report to identify key priority areas and the stakeholders needed to improve recruitment and retention	• Federal Department of Health (on behalf of the CTJWG)	• Next steps subject to consideration by all jurisdictions. Likely to be incorporated into future work plan
Collaboration across Clinical Trials Networks	• Clinical trial performance and metrics within Clinical Trials Networks reported by ACTA	• ACTA & NHMRC	• Major performance report released. Other reporting ongoing
Metrics and stakeholder input	• CTN / CTX now online	• TGA	• Implemented
	• NAS framework adoption is increasing	• CTJWG	• Interim Second Activity Report on Clinical Trials to be released in June 2017
	• Victoria internal and public benchmarks and metrics (e.g. time for streamlined ethical review)	• VIC government	• Implemented
Awareness of Australia as competitive clinical trial destination	• Searchable compilation of site capacity and capability	• NHMRC	• In development
	• Multiple campaigns / actions aimed at promoting Australia as a clinical trial destination	• Various sector participants (e.g. Austrade, AusBiotech, CTJWG, MTPConnect etc.)	• Ongoing
Supporting infrastructure and capability for clinical trials	• Refreshed approach to regional design and streamlined administration of clinical trial systems	• All jurisdictions via the COAG Health Council, aligned with Federal Budget measure	• In progress
	• Grants / funding to support infrastructure development	• QLD and NSW governments	• Awarded and ongoing

Initiative category	Key achievements	Major contributors	Status
	• Resources and tools to provide support for trial design, bioinformatics and collaboration	• NSW and VIC governments, ANZCTR	• Ongoing
	• Clinical Trials and Data Centre, and an infrastructure program	• WA government	• Implemented/ongoing
Other state and territory initiatives	• Funding for trials or trial coordinators / liaison officers	• QLD, NSW & WA governments	• Awarded and ongoing
	• Improved infrastructure / procedures to improve efficiency	• ACT & WA governments	Ongoing

These initiatives have made, and will continue to make, significant progress towards improving and maintaining Australia's international competitiveness as a clinical trial destination, when it comes to the efficiency of conducting a trial. Ongoing coordination and collaboration between governance stakeholders and sector participants is vital to ensuring the successful implementation of these initiatives. However, equally important is comprehensive dissemination and to ensure uptake of many of these initiatives throughout the various public and private participants in the sector.

To further support the Australian clinical trial sector, state and territory governments, the Department of Health, DIIS, and the NHMRC have worked to identify and continue to implement the next wave of priorities to improve Australia's international competitiveness as a destination of choice for clinical trials. These include implementing a refreshed approach to regional design and streamlined administration of clinical trial systems; facilitating a nationally consistent approach to the way clinical trials are overseen and conducted; establishing a metrics system and promoting Information and Communications Technology (ICT) interoperability; and strategically positioning Australia as a preferred location for clinical trials.

These initiatives are already having an impact. The TGA's CTN / CTX scheme is often recognised as one of the fastest and most efficient regulatory processes for clinical trials globally. And the NMA scheme has been identified as a key enabler for clinical trials in Australia.[89] For trials approved under the NMA scheme, ethics approval is now largely on par with international competitors. However there is still potential for Australia to improve its capabilities and its performance in the efficient conduct of clinical trials. As the global competition for clinical trials continues to increase, these improvements will be vital to maintaining Australia's competitive position.

[89] Australian Government Department of Health, Analysis of Recently Conducted Clinical Trials, 2015

6 Priorities for the future

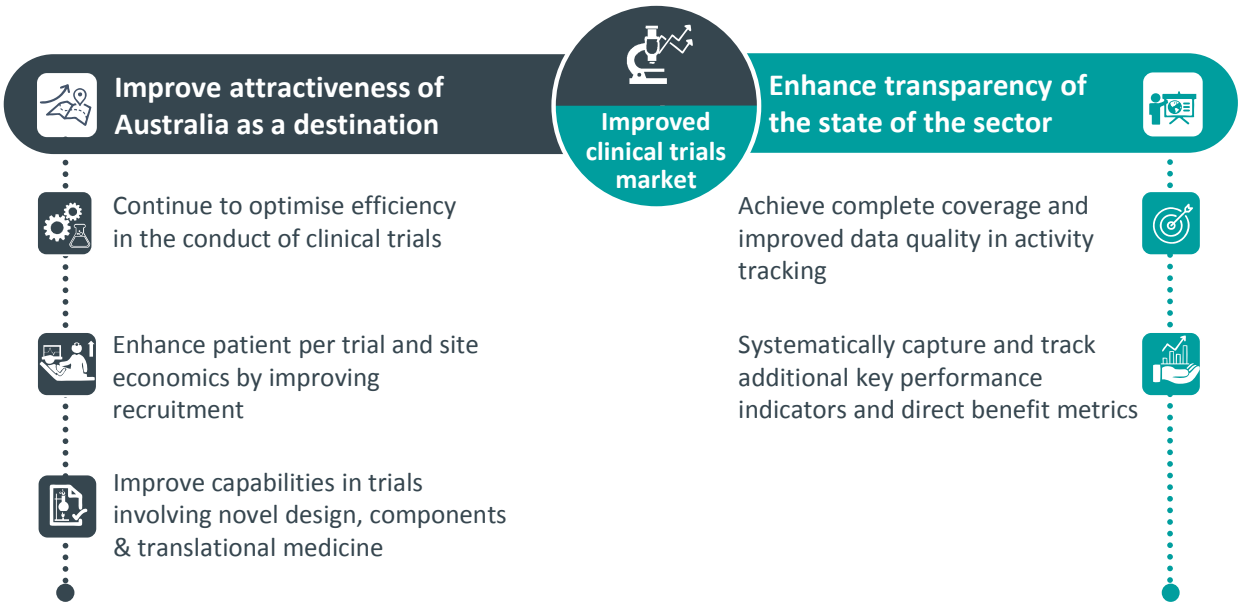
This report has aimed at providing a comprehensive audit of the state of the clinical trials sector, the value it provides and the competitive position Australia takes internationally. These final chapters provide an outlook for the sector assuming continued improvements can be made to achieve step-change growth in activity and expenditure. The CTAG report outlined an ambitious list of initiatives, the majority of which have been driven by state and federal governments. However, the continued success and improvement of the sector is reliant upon a collaborative approach between all stakeholders: government, sponsors, clinical investigators, health system managers and industry.

While it is evident that the sector and its stakeholders have made strides especially in improving processes towards more efficient conduct of clinical trials, MTPConnect has identified a number of priority areas for further improvement. These have been grouped under two overarching themes that relate to the scope of this report as well as the overall success of the sector going forward:

1. Improve the attractiveness of Australia as a clinical trials destination: *What activities are key to building a sustainable competitive edge in targeted areas?*
2. Enhance transparency / visibility of the state of the clinical trials sector: *How can the sector track activity and performance more consistently to accurately assess the state and improvements of initiatives over time?*

Both themes are ultimately intertwined and can serve as a reinforcing positive feedback loop. The following two sections discuss five priority areas under these two themes (Figure 21) including potential pathways to achieve them. The intent of highlighting these priority areas is to provide directional guidance that will require further analysis on feasibility and implementation options.

Figure 21 Priority areas overview



6.1 Improve the attractiveness of Australia as a destination

As outlined in this report, Australia has established itself in key competitive pockets in the global clinical trials market. Nonetheless the analysis that has gone into this report has highlighted areas that need to be further strengthened to not only defend Australia's position but also work towards more sustainable competitive advantages.

6.1.1 Continue to optimise efficiency and governing processes in the conduct of trials

As highlighted in sections 2.3.7 and 5.2, Australia has made significant progress in improving key processes involved in the start up and governance of clinical trials. Further efforts to harmonise and streamline processes are key to achieving better and more predictable outcomes (e.g. removing the variability in start up times based on inconsistent governance approval processes).

Given a number of jurisdictions are not yet signatories to the NMA scheme, Australia lacks a single whole-of-sector system for ethics approval. Many sponsors still submit multiple applications for multi-site trials since some aspects of the subsequent governance process have become more complex under the NMA. It has also been noted that some trial sites are reluctant to take the lead role, and hence responsibility, for providing ethics approval due to a lack of understanding of the requirements.[90] It is anticipated that improvements to the regional design and administration of clinical trial systems will alleviate these issues to some extent.

A continued nationally coordinated approach is needed to support and optimise further efficiencies and standardisation in the conduct of trials. The recently published CTJWG / Department of Health report on "*Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials*"[91] identifies the need to clarify leadership roles and establish dedicated structures to improve clinical trial coordination across Australia. A collaborative leadership approach to continue improvements to the sector and address these issues is currently being progressed by jurisdictions through the COAG Health Council. The Australian Government is also working with states and territories under a $7 million initiative to further streamline trial operations and assist stakeholders, sponsors, investigators and participants to better engage with clinical trials.

Similarly, the sector should build upon the achievements of the NHMRC and CTJWG / NMAJWG and continue to streamline the processes involved in the start up of a clinical trial. In general, jurisdictions should continue to seek formats to work jointly with Clinical Trials Networks and other partners to drive coordinated change.

6.1.2 Enhance patient per trial and site economics by improving recruitment

As highlighted by analysis in this and other reports, Australia has historically faced challenges in participant recruitment. An improvement in this area is viewed as a key growth opportunity by the industry experts interviewed for this report. Australia has a structural disadvantage in its relatively small population. As a result, Australia must develop improved recruitment

[90] Australian Government Department of Health, Analysis of Recently Conducted Clinical Trials, 2015

[91] Federal Department of Health (on behalf of the CTJWG), Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials, 2016

efficiencies to continue to compete against other countries in the region with significantly larger patient pools. Increased patient recruitment has the potential to:

- improve the quantum of overall benefits that Australia receives from trials
- allow better meeting of recruitment targets and timelines
- reduce the per-patient cost of conducting trials through better distribution of fixed costs, ultimately leading to more trials in Australia

MTPConnect believes that there are three avenues to improve recruitment: working at the level of the patient, the physician and the sector. Patient recruitment can be improved through public education regarding the role of clinical trials and the benefits they offer. Referral rates can be improved by educating healthcare professionals about clinical trials occurring nearby or in their fields of expertise, as well as developing the right kinds of incentives to encourage their participation. A third avenue for success is more systemic, fully leveraging the rollout and potential of electronic medical records (EMR). EMRs could be linked across districts and states, making patient records available to trial sites looking to recruit. This would allow for referral 'pull' by trial site investigators. EMRs may also be integrated into trial protocols that would allow the updating of records for the benefit of the healthcare professional normally treating a patient. Importantly, MTPConnect supports the use of the full breadth of EMRs already available in the market, including the involvement of private healthcare software providers. Recognising the challenges facing the clinical trials sector, the CTJWG and Department of Health recently commissioned a report on "*Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials.*" [92] MTPConnect's suggested priorities for the future are supportive of and complementary to this report.

6.1.3 Establish sufficient capabilities and expert capacity in trials involving novel design types, components, translational medicine and proof of concepts

Finally, expert interviews for this report have highlighted a shortage of capabilities and expert capacity specifically in early stage biotechnology trials (e.g. immunotherapy) involving novel designs (e.g. adaptive trial design, the human challenge model) and those that focus on translational medicine. The market may currently be experiencing a market failure, where insufficient volume of trials does not create a sufficient incentive for expansion in these capabilities and resources. However, until these capabilities are available, Australia will struggle to attract the trial types that require them. While these shortcomings warrant further investigation, forward-looking strategic investment in capabilities and expert capacity in these areas can help establish a sustainable advantage in cutting edge research that will be less subject to the competitive forces of the commoditized market.

[92] Federal Department of Health (on behalf of the CTJWG), Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials, 2016

6.2 Enhance transparency of the state of the sector

This report also reinforces the need for clarity and transparency in relation to clinical trial activity and the broader state of the sector. Similarly, the Department of Health and CTJWG report identifies the need to expand on national clinical trial metric tracking.[93] This will not only serve all stakeholders' needs for visibility but also allow the tracking of progress in the priority areas to improve Australia's competitive advantage.

6.2.1 Achieve complete coverage and improved data quality in activity tracking

As highlighted earlier in this report, clinical trials activity in Australia is tracked by multiple distributed and fragmented data registries, none providing a complete and accurate view across the whole of the sector. Given that each data source is designed for a different purpose, it is challenging to develop an accurate view of the clinical trials market as a whole. In addition, the non-mandatory nature of key fields (e.g. phase / type) lead to limited data quality in the underlying datasets. This inhibits appropriate interpretation of activity across different sub-sectors as well as associated decision making. The pathway to complete coverage and much improved data quality may only be achievable through additional mandates in either of the two existing solutions: an expansion of the NAS across jurisdictions, sponsor types and trial sites would help to fill gaps in activity tracking. Alternatively, a general ethics mandate for all trials to register and update entries on ANZCTR would help realise this objective. Key challenges that need to be resolved in any implementation design are:

- the mandate for complete entries and incentives for updating should be the same throughout a trial
- data linkages and IT system differences between jurisdictions. Clinical trial coordination units and cross-jurisdictional working groups may have an important role to play in specialised data collection, linkage and analysis

Specific steps are also needed to address instances where data gaps or lack of data fields is limiting the ability of the sector to describe activity or support policy decisions. For example, the chronic lack of staging data to describe or track trials activity for the rapidly growing medical device sector should be urgently addressed.

6.2.2 Systematically capture and track key performance indicators and benefit metrics

Apart from improving data collection on quality of clinical trial activity, it is also imperative to implement the systematic collection of key performance indicators and metrics measuring the level of benefits flowing to the sector. Only the combination of the two will reveal a comprehensive view of the state of the sector and developments across time. MTPConnect suggests the following metrics and potential collection methods:

[93] Federal Department of Health (on behalf of the CTJWG), Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials, 2016

Table 8 Priority metrics, current and future sources

	Metric		Current source(s)	Potential future sources / data collection methods
Performance	**Trial activity**		• ANZCTR • NAS • TGA	• NAS: via public and private HRECs and standardised approvals • ANZCTR: expanded HREC requirement for registration and improvements in data cleaning
	Trial start up time (including ethics and site approval)		• NAS	• NAS (as per existing framework), and extension of the NAS to private sites
	Number of participants		• Range per trial provided in CTNs	• NAS, if HRECs incorporate targeted patients into submission and reporting
	Actual vs. targeted recruitment (%)		• ANZCTR (anecdotally)	• Standardised, recurring industry surveys (widespread, retrospective updating of voluntary registries such as ANZCTR is not considered practical) • Ultimate inclusion in the NAS is desirable but will require additional data collection at the site level
	Recruitment timeline (time from first patient in to last patient treated)		• ANZCTR (actual start and end date anecdotally)	• Standardised, recurring industry surveys (widespread, retrospective updating of voluntary registries such as ANZCTR is not considered practical) • Ultimate inclusion in the NAS is desirable but will require additional data collection at the site level
Economic Activity	**Expenditure**	*Industry*	• Non-systematic / irregular surveys	• Standardised, recurring industry surveys
		Non-Industry / NHMRC funding sources	• Partially through associations such as AAMRI and ACTA	• Mandated and consistent collection metric by trial sites, incorporated into NAS reporting • Federal / state budget data or reporting, if expenditures by the MRFF and other public sources are disclosed in greater granularity
	Employment	*Trial sponsors / industry*	• Estimates by initial firms	• Standardised, recurring industry surveys
		Trial-site / clinical	• Non-systematic one-off / limited survey	• Mandated and consistent collection metric by trial sites, incorporated into NAS reporting

MTPConnect acknowledges that the successful tracking of these metrics is subject to a number of implementation challenges that need to be further investigated as part of any dedicated program.

7 Clinical trial sector growth outlook

As this report has captured, the breadth of the clinical trials sector's economic footprint and the benefits arising from the conduct of trials are substantial. Continued focus on reforming the clinical trials sector and enhancing international competitiveness could deliver significant economic and healthcare benefits to Australia.

Historic volumes suggest that Australia is still experiencing growth in the total number of trials conducted. However, as the trial segment analysis in section 4.4 illustrates, Australia faces strong competition in some trial segments from established trial countries and evolving competitors (such as Asia, Eastern Europe and South America) who are improving their track record, medical expertise and clinical trial framework. Further, interviews with global decision makers suggest that, at least for global later stage trials, the opportunity of additional growth in the number of trials will be more challenging as Australia is already considered for many of these trials and has a smaller patient population than most direct competitor countries. Other stakeholders also observe a capacity shortage of both Clinical Research Associates (on the sponsor / trial management side) and Clinical Trial Coordinators (on the clinical / site side), two of the linchpin resources of clinical trial management and conduct, as a growth impediment.

To defend its position and continue to grow Australia must:

- continue to drive reforms, efficiencies and service offerings to maintain the current trajectory, addressing barriers such as cost per patient which limit trials from certain segments.
- strategically invest in its trial capacity and in existing and potential future areas of advantage

Focusing on building on areas of strength and continued policy and structural improvements can be the foundation of a step-change growth in trial volumes, annual expenditure and other economic factors. If Australia can maintain its historical growth in trial numbers and improve patient recruitment by 25%-50% on average across trials, the value of the sector could increase to approximately $2.1-2.5 billion and sector employment could increase to approximately 13,000-16,000 by 2025.[94]

Table 9 Growth scenario expenditure (impact of MRFF and BTF not considered explicitly) and employment

	2015	2025 scenarios	
		Low case	High case
Expenditure ($m)	1,095	2,080	2,530
Employment	6,900	12,900	15,600

The Medical Research Future Fund and the Biomedical Translation Fund are also poised to provide new sources of funding for clinical trials in the sector. As outlined in section 3.2.1, these funds have been designed to provide sustainable revenue streams for the sector and ensure

[94] For detailed methodology please refer to Appendix G. iii - Growth outlook

that strategic investments in medical research and innovation are being pursued. The BTF has been established with $500 million and the MRFF is expected to reach $20 billion by 2020-21. Based on the 2017-18 Federal Budget, $33 million of the initial MRFF disbursements of $65.9 million will be directed towards funding clinical trials or will contribute to initiatives that aim to encourage further clinical trials activity.[95]

These investments will continue to add momentum to the reform agenda and strengthen the overall output of the clinical trials sector.

[95] Australian Federal Budget 2017-18, Health Portfolio Budget Statement

Glossary of terms

AAMRI	Association of Australian Medical Research Institutes
ACTA	Australian Clinical Trials Alliance
AHMAC	Australian Health Ministers' Advisory Council
ANZCTR	Australian New Zealand Clinical Trials Registry
ARCS	Association of Regulatory and Clinical Scientists
ARTG	Australian Register of Therapeutic Goods
ATC	Anatomical Therapeutic Chemical Classification System
AusBiotech	Australia's Biotechnology Organisation
BTF	Biomedical Translation Fund
CAGR	Compound Annual Growth Rate
COAG	Council of Australian Governments
CRA	Clinical Research Associate
CRO	Contract Research Organisations
CTAC	Clinical Trials Advisory Committee
CTAG	Clinical Trials Action Group
CTJWG	Clinical Trials Jurisdictional Working Group
CTN	Clinical Trial Notification Scheme
CTX	Clinical Trials Exemption Scheme
DIIS	Department of Industry, Innovation and Science
eCTN	Electronic Clinical Trial Notification
e-health	Electronic health (records)
FDA	US Food and Drug Administration
FTE	Full-time Equivalent
FTIH	First Time in Human (trials)
GCP	Good Clinical Practice
HPC	Hospitals Principal Committee
HREA	Human Research Ethics Application
HREC	Human Research Ethics Committee
HRQoL	Health-related quality of life
ICT	Information and Communications Technology
IHPA	Independent Hospital Pricing Authority
IIT	Investigator-Initiated Trial
IND	Investigational New Drug Application (US FDA)
IVD	In-Vitro Diagnostics Australia
KOL	Key Opinion Leader
KPI	Key Performance Indicator
MA	Medicines Australia
MOU	Memorandum of Understanding
MRFF	Medical Research Future Fund

MRI	Medical Research Institute
MTAA	Medical Technology Association of Australia
MTP	Medical technologies, biotechnologies and pharmaceuticals
NAS	National Aggregate Statistics
NHMRC	National Health and Medical Research Council
NIH	National Institute of Health (US)
NMA	National Mutual Acceptance Scheme
NMAJWG	National Mutual Acceptance Jurisdictional Working Group
PBS	Pharmaceutical Benefits Scheme
PIC	Pharmaceutical Industry Council (disbanded)
QALY	Quality-Adjusted Life Year
R&D	Research & Development
RGS	Research Governance Service
SEBS	Southern Eastern Border States
SSA	Site Specific Assessment (Governance)
TA	Therapeutic Area
TGA	Therapeutic Goods Administration
VET	Vocational Education and Training
WAHTN	WA Health Translation Network
WHO	World Health Organization

References and Consultations

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Access Economics	The Value of Investing in Health R&D in Australia	2008
Access Economics	Returns on NHRMC funded Research and Development	2011
ARCS Australia	A Needs Analysis for Education and Training Personnel Involved in Clinical Trials	2013
Association of Australian Medical Research Institutes	Members Report, 2016	2016
Austrade	Clinical Trials	2015
Australian Clinical Trials Alliance	Report on the Activities & Achievements of Clinical Trials Networks in Australia 2004-2014	2015
Australian Clinical Trials Alliance	Economic evaluation of investigator-initiated clinical trials conducted by networks	2017
Australian Clinical Trials Alliance	Submission to the NHMRC: Refinement of the Standard list of items associated with conducting Clinical Trials in Australia. Draft Final Report - Incorporating the Revised List	2014
Australian Government	Biomedical Translation Fund Factsheet	2016
Australian Government	National Research Infrastructure Capability Issues Paper	2016
Australian Government Department of Health	Analysis of Recently Conducted Clinical Trials	2015
Australian Government Department of Health	Scoping and analysis of recruitment and retention in Australian clinical trials	2016
Australian Medical Research Advisory Board	Australian Medical Research and Innovation Strategy 2016-2021	2016
BioNJ	Economic Impact Study of Clinical Trials Activity in New Jersey	2016
Bureau of Economic and Business Research, University of Florida	The Economic Impact of the University of Florida's Clinical and Translational Science Institute	2013
Canadian Clinical Trials Coordinating Centre	Clinical Trials – the Canadian Advantage	2016
Clarke & Loudon	Effects on patients of their healthcare practitioner's or institution's participation in clinical trials: a systematic review	2011
Clinical Trials Action Group	Clinically Competitive: Boosting the Business of Clinical Trials in Australia	2011
Clinical Trials Advisory Committee	Terms of Reference	2014

Clinical Trials Jurisdictional Working Group	Sydney and Melbourne Industry Liaison Meetings	2015
Clinical Trials Jurisdictional Working Group	Clinical Trials Jurisdictional Working Group Framework for National Aggregate Statistics (NAS) Second Activity Report on Clinical Trials in Australian Public Health Institutions (2015-16)	2017
Commonwealth of Australia	Federal Budget 2017-18	2017
Council of Australian Governments	Communique 24 March 2017	2017
D. Andrews et al.	Intangible Assets, Resource Allocation and Growth - A Framework for Analysis	2012
Dr. Robert Herkes	ACTA Summit 2016 – What we know about the health and economic benefit of trials and registries in Australia	2016
Independent Hospital Pricing Authority	Determination of standard costs associated with conducting clinical trials in Australia	2015
Innovation and Science Australia	Performance review of the Australian Innovation, Science and Research System	2016
Hunt, The Hon. Greg (Minister for Health and Minister for Sport)	Delivering $33 million to help fund our next medical breakthrough	2017
Hunt, The Hon. Greg & Sinodinos AO, The Hon. Arthur (Minister for Industry, Innovation and Science)	First BTF investment aims to improve lives through innovation	2017
KPMG	NIHR Clinical Research Network: Impact and Value Assessment	2016
Lateral Economics	The Economic Value of Australia's Investment in Health and Medical Research: Reinforcing the Evidence for Exceptional Returns	2010
M. Clarke, et al.	Effects on patients of their healthcare practitioner's or institution's participation in clinical trials: a systematic review	2011
M.K. Krzyzanowska, et al.	How may clinical research improve healthcare outcomes?	2011
Medical Technology Association of Australia	Guidelines for Compensation for Injury Resulting from Participation in a Company Sponsored Clinical Investigation	2010
Medicines Australia	Keeping Clinical Trials in Australia - Why Action is Needed	2011
Medicines Australia	Clinical Trial 'Metrics': Benchmarking Australia's Performance	2014
Medicines Australia	FactsBook – Fourth Edition	2015

Medicines Australia and Pharmaceutical Industry Council	Clinical Trials in Australia - A Report on the Characteristics of the Clinical Trials Industry in Australia	2010
National Health and Medical Research Council	Good Practice Process for Site Assessment and Authorisation Phases of Clinical Trials Governance	2016
National Health and Medical Research Council	Report on the Activity of Human Research Ethics Committees for the period: 1 January 2014 to 31 December 2014	2015
National Health and Medical Research Council	National Certification Scheme - Institutions with certified ethics review processes	2016
New South Wales Clinical Trials Business Development Centre	Inaugural Survey of Investigator Perceptions on the Value of Industry Funded Clinical Research	2009
New South Wales Ministry of Health	NSW Health and Medical Research Strategic Review	2012
New South Wales Office for Health and Medical Research	NSW Metrics for Health and Medical Research, including Clinical Trials	2016
Organisation for Economic Co-operation and Development	Gross domestic expenditure on R-D by sector of performance and field of science	2017
Pharmaceutical Research and Manufacturers of America	Biopharmaceutical Industry-Sponsored Clinical Trials: Impact on State Economies	2015
Pharmaceuticals Industry Council	2011 Survey of Privately Funded Clinical Research Activity	2012
Pharmaceuticals Industry Council / C. Bourgeois	Assessing the Value of Industry Sponsored Clinical Trials	2009
Pharmaceuticals Industry Strategy Group	Final Report	2008
Productivity Commission	Public and Private Hospitals	2009
Pugatch Consilium	Race for Biopharmaceutical Innovation	2016
R.M. Calif, et al.	Characteristics of Clinical Trials Registered in ClinicalTrials.gov 2007-2010	2012
S. McKeon, et al.	Strategic Review of Health and Medical Research in Australia	2013
S.C. Johnston	Effect of a US National Institutes of Health programme of clinical trials on public health and costs	2006
S.R. Majumdar, et al.	Better outcomes for patients treated at hospitals that participate in clinical trials	2008
Southern Star Research	The Australian Clinical Trials Environment	2016
Therapeutic Goods Administration	Access to Unapproved Therapeutic Goods – Clinical Trials in Australia	2004
Therapeutic Goods Administration	Introduction to changes to the TGA's Clinical Trial Notification (CTN) process	2015

Victorian Government	Healthier Lives, Stronger Economy - Victoria's Health and Medical Research Strategy 2016-2020	2016
World Health Organization	Statement on Public Disclosure of Clinical Trial Results	2015
W. Van Gijn, et al.	Quality assurance in rectal cancer treatment in the Netherlands: a catch up compared to colon cancer treatment	2010

Consultations

Category		Entity
Private sector	Industry Associations	AusBiotech
		Medicines Australia
		MTAA
		AAMRI
		ARCS Australia
	Industry (Biopharma)	CSL Australia
		Novartis Australia
		Roche Australia
		Global Pharmaceutical Company Representative #1*
		Global Pharmaceutical Company Representative #2*
		Global Pharmaceutical Company Representative #3*
	Industry (Medtech)	Abbott Australia
		Medtronic Australia
		Sirtex Australia
	Industry (CROs)	CMAX
		Five Corners
		Linear
		Novotech
		PPD
		QuintilesIMS
		Southern Star Research
MRIs		Baker IDI / Nucleus Network
Not-for-profits		ACTA
		Bellberry
		PRAXIS
Public sector		ANZCTR
		Austrade
		CTJWG
		Department of Economic Development Victoria
		Department of Health – Commonwealth
		Department of Health – Victoria
		Department of Industry, Innovation and Science
		NHMRC
		Northern Sydney Local Health District
		OHMR
		St. Vincent's Hospital
		The Royal Melbourne Hospital
		TGA

Note: * Interviews were conducted with regional or global executives from several multinational medtech and pharmaceutical companies regarding their selection criteria for locating trials. These individuals preferred not to have their company names published.

Appendix A. Current state of initiatives

This appendix further details the range of initiatives within the sector that are addressing reform recommendations or generally aiming at improving the conduct and competitiveness of clinical trials in Australia.

i. Timeliness of ethics and research governance

Previous reports have raised concerns about the considerable variability in how long it takes for clinical trials to begin in Australia, relative to other countries.[96] Australia has advantages at a national level in the form of risk-based regulations that can improve trial start up times (e.g. the CTN scheme) however, this overall advantage can often be eroded at a site level. A proposal to start a trial requires approval from an HREC and site authorisation (including a governance review). Sponsors running multi-site trials often needed to complete multiple applications, increasing the time, and often cost, to commence a trial. Some sponsors still submit multiple applications, even though they don't actually need to. The time to obtain HREC and governance approval often varies between sites, increasing the uncertainty for trial sponsors.

Table 10 Summary of initiatives to improve ethics and governance

Initiative title	Responsible	Description	Status
National Mutual Acceptance (NMA) Scheme	• State governments party to the NMA Memorandum of Understanding (MOU)	• The NMA aims to achieve acceptance of single ethics review across all sites involved in a trial, reducing duplication and trial start up times • All state and territory departments have agreed to an MOU for mutual acceptance of scientific and ethical review	• NSW, QLD, VIC, SA & ACT have signed to-date. WA has committed to participate by July 2017
	• Ethics committees associated with Public Health Organisations in NMA-jurisdictions • NHMRC	• Institutions eligible to participate in NMA must have been certified by NHMRC under the National Certification Scheme for institutional ethics approval processes and approved by the jurisdictions participating in NMA	• There are plans to extend the NMA Scheme to private ethics committees & universities[97]
Other state and territory government initiatives	• NSW Government	• NSW has implemented a reform process including requirements for preapproval of research, data collection and reporting	• Underway
	• NSW Government	• NSW is developing a Research Ethics and Governance Information System to manage applications, and monitor and report all human research including clinical trials. A systems provider has been selected	• Ongoing
	• NSW Government	• NSW is undergoing consultation to streamline the SSA process of governance approval	• Ongoing

[96] Medicines Australia, Keeping Clinical Trials in Australia - Why Action is Needed, 2011; Australian Government Department of Health - Analysis of Recently Conducted Clinical Trials, 2015

[97] Confirmed through discussions with the Federal Department of Health in 2017

	• VIC Government	• VIC is providing $1.3m per annum for the Streamlining Clinical Trials Research Program including developing new data management and reporting systems for timeliness and activity and promote streamlined approach[98]	• Ongoing
	• QLD Government	• QLD has established a web based Central Coordinating Service and provided $9.5m to fund Cancer Clinical Trial Coordinators from 2006-2020	• Ongoing
	• NT Government	• NT is prioritising work to streamline ethics and governance reviews including SSAs, moving towards administration through one office	• Ongoing
	• WA Government	• WA developed a Research Governance Service (RGS) IT system, which captures required metrics for clinical trials and incorporates all relevant application forms and governance information, including recruitment, funding and IHPA standard costs	• Complete
	• WA Government	• WA appointed Clinical Trial Liaison Officers in the public health system. A reporting module for clinical trials is being built into RGS, with standard forms and processes to allow for ethics / governance review in parallel	• Underway
	• WA Government	• WA has provided $1.3m to establish a Clinical Trials and Data Centre and has provided ongoing funding for the development of Research Education and Training online modules, including GCP	• Ongoing
	• SA Government	• SA is working towards improved governance efficiency, clinical trial metric reporting and is investigating the feasibility of a central coordinating unit for trials in SA	• Ongoing
	• State governments	• QLD, NSW, VIC and SA formed Southern Eastern Border States (SEBS) committee to facilitate coordinated review of amendments to MA and Medical Technology Association of Australia (MTAA) Clinical Trials Research Agreements	• Complete
Cross-jurisdictional collaboration	• CTJWG	• Coordinated federal and state activities that aim to enhance consistency, improve navigation and streamline the conduct of clinical trials	• Ongoing
	• Federal regulatory bodies and the TGA	• The TGAs CTN / CTX scheme for clinical trials involving unapproved drugs or devices	• Implemented and highly effective
	• ACT	• Working with jurisdictions and universities to streamline cross-institutional research governance	• Ongoing
	• ACT	• Expanding Clinical Trials Unit across public health trials sector to facilitate coordination	• Ongoing

[98] VIC Government, Healthier Lives, Stronger Economy - Victoria's Health and Medical Research Strategy 2016-2020, 2016

Various NHMRC initiatives	• NHMRC, state governments, various ethics committees and trial sites	• Web based common ethics applications for human research (HREA) and national certification schemes for institutional ethics approval processes	• Released on 14 Dec. 2016. There are currently 4,000 registered users
	• NHMRC	• Establishment of two independent committees to support complex human ethics reviews	• Complete

Current status

Following the implementation of initiatives surrounding ethics approval, Australia is deemed to have one of the fastest ethics approval processes in the world. There are numerous recent examples in oncology, Phase I studies, and general / primary care in the private sector that have achieved sufficient or leading start up times. However, Australia still lacks a national system for ethics approval and many sponsors still submit multiple applications for multi-site trials since some aspects of the subsequent governance process has become more complex under the NMA. It has also been noted that some trial sites are reluctant to take the lead role, and hence responsibility, for providing ethics approval due to a lack of understanding of the requirements.[99] While ethics approval processes have seen considerable improvements, governance has not yet seen the same level of harmonisation or unification, and thus varies considerably across trial sites. It is often cited as the cause of start up delays for clinical trials and further observations by sector participants suggest that contrary to recommendations following the CTAG report, sites do not process ethics reviews in parallel with governance applications, contributing to the lengthening of the trial start up process.

ii. Education and training

The sector has been supported by a number of education and training initiatives for professionals overseeing clinical trials to assist in streamlining the administration processes. While there are courses offered by higher education organisations and industry groups, they predominately focus on regulations and good practice procedures, and not necessarily the skills needed to run a clinical trial.

Many research governance officers who oversee clinical trials at the site level are trained 'on the job', and skills and competencies vary between organisations. It has been suggested that there is a need for a national understanding of competencies required by research governance officers who process applications and the researchers who write them.

[99] Australian Government Department of Health - Analysis of Recently Conducted Clinical Trials, 2015

Table 11 Summary of initiatives to improve education and training

Initiative title	Responsible	Description	Status
VET accredited course for governance officers and clinical researchers	• Swinburne University	• Vocational Education and Training (VET) accredited course was developed by the Department of Industry, innovation, Climate Change, Science, Research and Tertiary Education, informed by a needs analysis conducted by ARCS Australia [100]	• Pilot training sessions were completed in 2015, but the course has not been widely used
	• PRAXIS	• In partnership with RMIT, PRAXIS provides VET accredited education to the HREC sector in Australia	• Ongoing, 25% of all HREC members are now trained under this model
Competency framework for professionals involved in academic trials	• PRAXIS	• PRAXIS, with its partner Harvard MRCT, developed a Research Essentials program for all elements of the research workforce, with a specific emphasis on clinical trials and a competency based training model for Research Governance Officers	• Available for ongoing enrolment
	• NHMRC	• In conjunction with ACTA, NHMRC is developing a competency and training framework for investigators conducting non-commercial trials • An initial workshop was held in August 2015	• Draft competencies are planned to be released for targeted consultation in March 2017
Clinical trials e-learning modules	• NHMRC	• Three e-learning modules were developed to provide information on the clinical trials environment and ethics / governance reviews	• Currently available on Australian Clinical Trials website
	• PRAXIS	• PRAXIS has developed a number of ethics-focused e-modules for clinical trials, offered in the form of short courses and workshops / webinars	• Ongoing
Further toolkits and training courses	• VIC Government	• Coordinating Office in Victoria hosts targeted forums and workshops to inform the sector	• Ongoing since 2009
	• WAHTN	• WA Health Translation Network (WAHTN) has developed online TransCelerate recognised GCP Modules	• Ongoing
	• ARCS	• ARCS offers applied GCP training (both online and face-to-face) which are TransCelerate recognised as well as forums, seminars, workshops and communities to assist with the application of knowledge in the workplace	• Ongoing
	• ARCS	• ARCS also assists government with provision of free online education in support of critical initiatives affecting the clinical trial landscape	• Ongoing

Current status

While the activities to address education and training have demonstrated momentum, the uptake and impact of these initiatives within the sector is not sufficiently tracked.

iii. Standard costs for clinical trial activities

The CTAG report noted a high variability in the fees charged for clinical trial items, such as ethics and governance applications. It also identified that prices for common activities differ greatly

[100] ARCS Australia, A Needs Analysis for Education and Training Personnel Involved in Clinical Trials, 2013

between industry and non-industry sponsored trials. The report recommended a national approach to developing charges for clinical trials to ensure transparency and increase certainty on the costs of clinical trials.

Table 12 Summary of initiatives to introduce standard costs for clinical trials

Initiative title	Responsible	Description	Status
Standard table of costs for conducting clinical trials in Australia [101]	• IHPA	• IHPA developed a table of standard costs for a list of activities compiled by the NHMRC. Following further reviews it developed a revised list with prices for 42 activities	• Final revised tables published in 2015 but have not been adopted by whole-of-sector

Current status

The table of standard costs was developed as a guide to assist in negotiating clinical trial budgets and to provide greater clarity for sponsors, noting that negotiation of trial budgets is a matter for sites and sponsors. Despite its release, some concerns remain about the costing of clinical trials including:

- whether the list reflects the true cost for some items
- how to separate trial specific costs from standard care
- difficulties with the costing of research activity
- the list predominately contains items for pharmaceutical trials, so its usefulness for other trial types is limited (e.g. medical technology trials)

iv. Patient recruitment for clinical trials and e-health

In Australia, the majority of participants for clinical trials are recruited through the investigator or by patient referrals. Other less common methods include consumer friendly websites, individual electronic health records or community-based approaches such as patient advocacy groups. A number of reports (e.g. Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials [102], CTAG Report [103]) have highlighted difficulties in recruiting participants for clinical trials in Australia.

Table 13 Summary of initiatives to improve patient recruitment and e-health

Initiative title	Responsible	Description	Status
IT infrastructure	• DIIS • NHMRC • ANZCTR	• DIIS and NHMRC, with input from a joint industry & jurisdictional committee, have developed a clinical trials portal (www.australianclinicaltrials.gov.au) with information about trials in Australia, including an alert service for individuals interested in certain trials	• Portal released with notification and subscription service added in 2015
	• ACT Government	• Developing an IT infrastructure to support clinical trials and enhance patient recruitment	• Ongoing

[101] IHPA table of standard costs - *https://www.ihpa.gov.au/publications/development-table-standard-costs-conducting-clinical-trials-australia*

[102] Federal Department of Health (on behalf of the CTJWG), Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials, 2016

[103] Clinical Trials Action Group, Clinically Competitive: Boosting the Business of Clinical Trials in Australia, 2011

	• WA Government	• Developing RGS to publish all recruiting clinical trials	• Under development
E-Health records for patient recruitment	• Australian Digital Health Agency and Federal Department of Health	• A major recommendation of the CTAG report was to ensure that Australia's e-health records were linked to clinical trial databases and used to enhance patient recruitment • Uptake of e-health in Australia has been slow. Capacity to utilise electronic patient records to support clinical trial recruitment will ultimately be determined by the overall Digital Health Agenda	• The Digital Health Agency is currently seeking input into better use and integration of e-health
Consumer information and education	• Cancer Australia	• Cancer Australia developed a series of web-based modules to educate consumers about clinical trials	• Complete
	• Consumers Health Forum	• With support from DIIS and NHMRC, the Consumers Health Forum developed a brochure explaining the process and costs of participating in trials	• Complete
	• NHRMC & CTJWG	• Clinical trials marketing campaign targeting GPs, clinicians and patients	• To be launched
Review of patient recruitment technologies	• Federal Department of Health (on behalf of the CTJWG)	• Scoping and Analysis of Recruitment and Retention in Australian Clinical Trials report to identify key priority areas and the stakeholders needed to improve recruitment and retention	• Next steps subject to consideration by all jurisdictions. Likely to be incorporated into future work plan

Current status

While initiatives such as these have made inroads, especially from a consumer facing perspective, challenges around recruiting patients for clinical trials remain, and improving recruitment rates continues to be an objective for the clinical trials sector. A lack of GP and public awareness of clinical trials, poor referrals between clinicians and sub-optimal e-health system usage continue to limit the efficiency and success of patient recruitment in Australia.

v. Collaboration across Clinical Trials Networks

Clinical Trials Networks have been essential in the development of the sector. With the majority of the networks having formed in the last ten years, CTAG identified the need to create transparency on the activity of networks by first creating an inventory of networks. Secondly it was deemed beneficial to further consolidate and foster efforts of coordination across academia, clinical medicine and industry.

Table 14 Summary of initiatives to improve collaboration across Clinical Trials Networks

Initiative title	Responsible	Description	Status
ACTA initiatives	• ACTA • NHMRC	• NHMRC had provided funding to ACTA to support its annual symposium and to collect and report metrics within Clinical Trials Networks	• Major performance report released in 2015, other reporting ongoing
	• Federal Department of Health • ACTA	• MRFF Lifting Clinical Trials and Registries Capacity – Grant Program - $5 million over four years to support ACTA and build the capacity of existing and new Clinical Trials Networks	• Announced May 2017

Current status

Whilst ACTA and other Clinical Trials Networks are currently supported, there is a need to ensure ongoing finances to foster collaboration in the sector. In a media release following the publication of the FY18-19 Federal Budget, the Minister for Health indicated that $5m would be allocated to ACTA over four years, "to support their work in ensuring Australia maintains its world leading clinical trial standards and continues to support the clinical trials sector".[104]

vi. Metrics and stakeholder input

Historically, data on clinical trials in Australia and the wider health sector has been collected across a number of platforms with different purposes:

- as outlined earlier in this report, the TGA collects metrics on clinical trials testing drugs or devices not approved for the trial specific use in Australia, but it does not collect any post-approval trial performance metrics.
- each of the States and Territories compiles data on clinical trials carried out in their jurisdiction, including metrics on administrative processes, which are now published in the NAS (for participating jurisdictions). However, the data collected is not entirely consistent between jurisdictions, does not cover all jurisdictions, excludes trials conducted in private sites, and is yet to cover metrics such as investment or employment
- it is becoming a more stringent requirement for clinical trial investigators to register their clinical trial on a registry site such as the ANZCTR or clinicaltrials.gov in order to publish their results.[105] These registries rely on investigators to enter and regularly update their entries, which is not common practice in all segments of the sector.

A number of recent sector reports have highlighted the need for reliable, accessible data about clinical trials in order to monitor the progress of clinical trial activities in Australia, including jurisdictional data on the timeliness of ethics and governance reviews.

Table 15 Summary of initiatives to develop sector metrics and stakeholder input

Initiative title	Responsible	Description	Status
Online CTN form	• TGA	• In 2015 the TGA released an online version of the old paper based CTN form	• Complete – ongoing efficiencies and data reporting being sought
National Aggregate Statistics framework and report	• CTJWG	• The CTJWG developed the NAS framework of a minimum standard of metrics to be collected across jurisdictions for industry sponsored trials, collecting data to measure performance, the success of reforms and identify areas of improvements	• Second Activity Report on Clinical Trials to be released in June 2017
	• NHMRC • TGA • Bellberry	• The NHRMC, TGA and Bellberry are aiming to collect data for trials completed in private hospitals	• Ongoing

[104] Media release by the Hon. Greg Hunt, "Delivering $33 million to help fund our next medical breakthrough" (19/05/2017)
[105] World Health Organization, Statement on Public Disclosure of Clinical Trial Results, 2015

Collection of ethics committee data	• VIC Government	• Victoria internal and public benchmarks and metrics (e.g. time for streamlined ethics review)	• Implemented

Current status

Though some progress has been made on collecting clinical trials data in Australia, the data that is collected remains partial and does not yet provide a reliable, comprehensive and accessible dataset to evaluate the overall performance of the sector (see sections 2.3 and 6.2 for details).

vii. Awareness of Australia as a competitive clinical trial location

Despite the key role of clinical trials within the overall healthcare system, local trial success stories are not well known or heavily publicised locally or globally, to either potential sponsors / investigators or to potential participants. Various initiatives have aimed at improving the public profile to attract attention to success stories, reform progress and stimulate further participation.

Table 16 Summary of initiatives to increase awareness of Australia as a clinical trial location

Initiative title	Responsible	Description	Status
Clinical Trials Ready Initiative	• NHMRC	• NHMRC is looking to develop criteria that may be used as a means to recognise site capacity and capability. Once assessed, trial sites would be showcased and advertised to potential sponsors	• In development
Promoting Australia as a clinical trial destination	• Austrade • CTJWG • MTPConnect • Peak industry bodies (e.g. AusBiotech) • Life Sciences Queensland	• Multiple organisations have undertaken initiatives and actions to advertise and promote Australia as a destination for clinical trials, including a capability report, marketing campaigns, promotional websites and engagement with decision makers in global multi-national companies	• Ongoing

Current status

Stakeholder engagement for this report highlighted that there is limited awareness even amongst informed industry participants about the latest status of some reforms and what has been achieved. This suggests that further awareness raising and outreach is necessary.

viii. Supporting infrastructure and capability for clinical trials

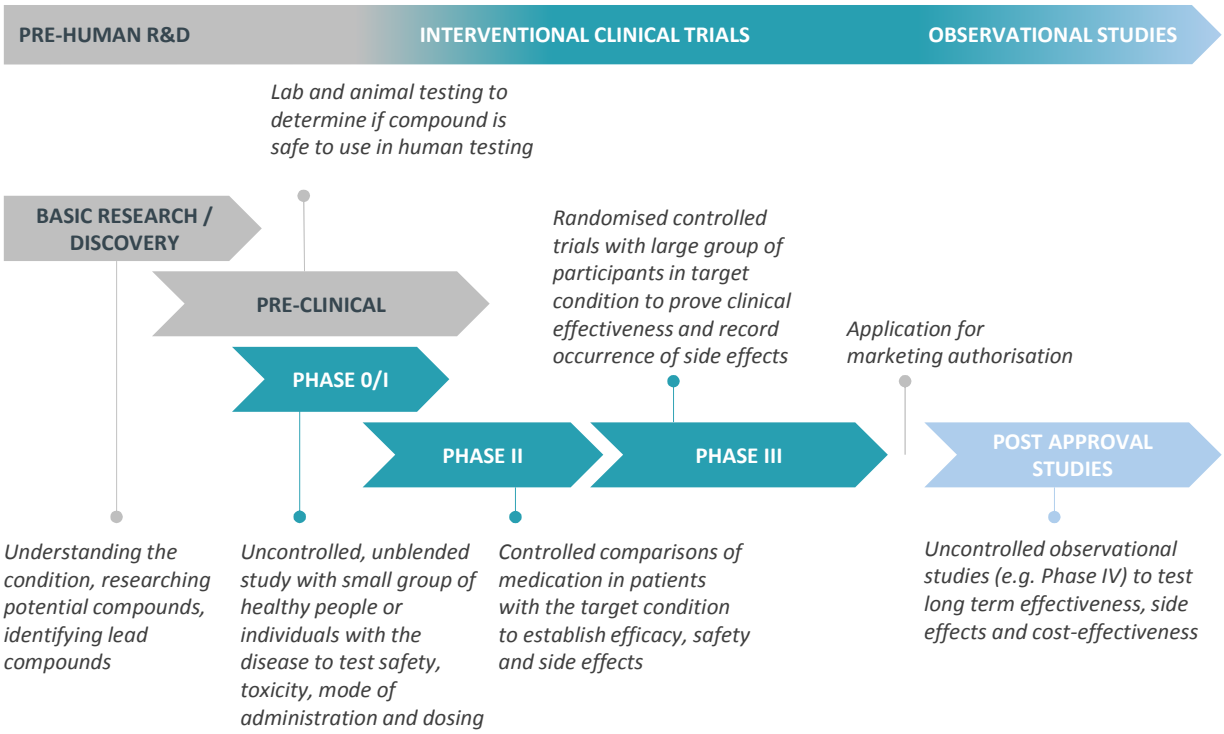
Table 17 Summary of initiatives to support trial infrastructure and capability

Initiative title	Responsible	Description	Status
	• QLD Government	• $18.9m annually to QIMR Berghofer, who own QPharm Pty Ltd, conducting early phase trials	• Ongoing
	• NSW Government	• Grant to establish Scientia, a Phase One Clinical Trial Centre at University of NSW	• Ongoing
	• NSW Government	• $9m over four years for medical cannabis trials	• Ongoing

Clinical Trial Infrastructure	• NSW Government	•	$12m to support state wide biobank facility. In 2014 a state wide biobanking service delivery model commenced; developing certification, MTAs and a specimen locator	• Ongoing
	• MTPConnect / COSA	•	$115k tele-health strategy to increase patient access to cancer clinical trials	• Ongoing
	• WA Government	•	Infrastructure support through the Medical and Health Research Infrastructure Fund and Research Institute Support	• Ongoing
	• NHMRC / ANZCTR	•	NHMRC provided funding to ANZCTR in 2016 to support its continued operation	• Complete
	• All jurisdictions via the COAG Health Council	•	Aligned with Federal Budget measures, all jurisdictions are developing a refreshed approach to regional design and streamlined administration of clinical trial systems	• In progress
Capability support	• NSW Government	•	Providing online resources and toolkit, clinical trial design unit and quality assurance programs	• Ongoing
	• NSW Government	•	Bioinformatics training for clinical researchers and training for technical staff	• Ongoing
	• NSW Government	•	The NSW Office for Health and Medical Research is developing a framework and guidelines for the conduct of early phase clinical trials within NSW	• Ongoing
	• VIC Government	•	Developing a clinical trial registry to enable collaboration and promote expertise and capacity	• Ongoing
	• WA Government	•	$1.3m to establish a Clinical Trials and Data Centre under WAHTN to streamline processes, utilise bioinformatics and data management capabilities and attract trials to WA	• Implemented / Ongoing
	• QLD Government	•	$9.4m to fund Cancer Clinical Trial Coordinators via Queensland Council	• Complete
	• SA Government	•	Support for the SA Academic Health Science and Translation Centre; focuses on improving SA clinical trial sector	• Ongoing

Appendix B. Clinical trials stage classification methods

Figure 22 The Phase I-IV Approach



The phases of clinical trials have distinct purposes and act as gatekeepers in bringing new products or treatments to market. Generally, the early phase clinical trials (Phase 0 / I to II) focus on testing safety and efficacy in humans. Phase III trials are more robust trials that use larger numbers of patients in randomised controlled trials to capture data on the effectiveness on clinical outcomes. Data from Phase III trials is used to satisfy requirements for regulatory approval. Post approval studies (e.g. Phase IV) are conducted after marketing authorisation. These trials are designed to monitor the long-term effectiveness and adverse effects of the approved intervention in the general patient population. Other purposes may include the investigation of the potential use of the intervention in a different condition, or in combination with other therapies.[106]

Medical device trials generally follow a different staging structure to interventional drug trials. Early stage medical device trials are often regarded as 'first in man', 'safety & feasibility' or 'pilot' studies that test the device in a small group of participants for safety and performance. If the feasibility of the device is proven, the sponsor elects to conduct a larger 'pivotal' study based on a trial protocol and a statistically meaningful number of participants. 'Post approval' studies similarly collect data on the long-term effectiveness of the intervention in a non-controlled environment.[107]

[106] National Health and Medical Research Council - *www.australianclinicaltrials.gov.au/what-clinical-trial*
[107] TGA, Access to Unapproved Therapeutic Goods – Clinical Trials in Australia, 2004

Appendix C. Trial data sources

A range of data sources exist to track clinical trial activity, however there is not one complete source of data. Each source has a different scope or purpose, and each comes with its own limitations that limit the interpretability of analysis on the data.

The TGA, a regulatory trial notification data source, defines clinical trials largely based on testing the safety of an intervention:

"*A planned study in humans of an intervention (including a medicine, treatment or diagnostic procedure) with the object of investigating safety or efficacy and designed to achieve at least one of the following: the discovery or verification of clinical, pharmacological and other pharmacodynamic effects, the identification of adverse reactions or adverse effects, the study of absorption, distribution, metabolism or excretion*" [108]

Trial registries such as the ANZCTR use the much broader World Health Organization definition of clinical trials:

"*For the purposes of registration, a clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes […] Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc*." [109]

The NAS, a jurisdictional ethics and research governance data source, uses a slightly narrower definition of clinical trials:

"*Interventional research involving a drug / device trial, radiation therapy, surgery, treatment or diagnostic procedure and studies associated with ongoing activities relating to trials that have been conducted. This may include post-trial activities such as observational research and evaluation of a trial, developing a registry and other post-marketing surveillance activities*" [110]

[108] Therapeutic Goods Administration Glossary - *http://www.tga.gov.au/acronyms-glossary*
[109] World Health Organization Glossary - *www.who.int/ictrp/glossary/en*
[110] Clinical Trials Jurisdictional Working Group Framework for National Aggregate Statistics Second Activity Report on Clinical Trials in Australian Public Health Institutions (2015-16)

Table 18 Summary of scope and limitations of clinical trial data sources

Data source	Scope / purpose	Limitations
TGA (2015 Australian trial volume = 953)	• Trials involving drugs / devices that are not registered on the Australian Register of Therapeutic Goods must be approved by the TGA • This approval process occurs through the CTN / CTX scheme and data is typically entered by the trial sponsor. This data is tracked and reported by the TGA • The data is purely captured for regulatory approval purposes and is only released at a highly aggregated level	• Does not capture trials for drugs / devices that are already approved • Incomplete time series due to transition from paper based system to online system. The TGA is not confident about the accuracy of pre-online entries • Includes all trials that were intended to be carried out, but is not updated or altered to reflect whether the trial actually started • Complete dataset is not publically available • Entry of patient recruitment numbers is not mandatory • Dataset includes some duplication of records due to the way the eCTN interacts with certain trial activities (e.g. use of multiple CROs / sites; change of therapeutic good). Refer to 0for further detail • Confidentiality of data provided to the TGA limits its usefulness as a public reporting source for clinical trial activity.
ANZCTR (2015 Australian trial volume = approx. 1,360)	• Voluntary Australian & New Zealand clinical trial registry that captures data about clinical trials conducted in Australia • Captures the full range of trials including industry trials, IITs and observational studies • Recognised by the WHO's International Clinical Trial Registry Platform as a Primary Registry • ANZCTR has recently added a feed from clinicaltrials.gov to supplement its own entries	• Does not capture all trials in Australia (particularly international trials that may be entered on international registries) • Historically seen by some sector participants as inaccurate due to entries not being updated to reflect what actually happened in the trial • Time series comparisons should be treated carefully since any growth reflects both changes in clinical trial volumes and an increase in registration compliance for existing trials, however non-compliance is believed to be less of an issue from 2012 onwards • Participant statistics are aggregated at the trial level, but are not broken down to the country or site level
Clinicaltrials.gov (2015 Australian trial volume = approx. 500)	• Clinical trials registry and results database managed by the NIH in the US • Contains public and private trials across the full range of trial and intervention types • Compulsory for all trials that fall under FDAAA 801 in the US to be registered	• US focused - does not capture all international studies for valid comparison • Australian trials are predominately industry / commercial trials, with limited coverage of Australian IITs and as a result only captures approximately 40% of clinical trial volume reported by ANZCTR
NAS (FY2015 Australian public health organisation clinical trial volume = approx. 700)	• Government clinical trial registry with data collected from jurisdictional ethics and research governance data • Captures data on clinical trials occurring in Australian publically funded hospitals across five jurisdictions (New South Wales, Northern Territory, Queensland, South Australia and Victoria)	• Does not capture private health organisations, universities or clinical trials conducted in primary care settings • Does not capture data from jurisdictions not reporting in NAS format or with incomplete data sets • Time series comparisons are not yet available

World Health Organization	• The WHO hosts a search portal to search numerous international clinical trials registries at the same time • It shows results from key registries including ANZCTR and clinicaltrials.gov	• Not a registry in its own right – trials are not actually registered with WHO • The same limitations apply as for the underlying registries that can be searched • Reconciliation is applied but cannot guarantee the removal of all duplicates
NHMRC data sources	• Annual and Completion reports submitted to NHMRC as a condition of funding (NHMRC funded trials only) • Data captured via the annual reports submitted by HRECs and certified institutions • Meta-data captured through the HREA (submitted applications only)	• Annual and Competition reports limited to NHMRC funded trials only • HREC annual reports may capture all clinical trials (as all clinical trials require ethics approval) but double counting is expected for trials approved by multiple HRECs • HREA only captures data from applications submitted through the system

Appendix D. Analysis of clinicaltrials.gov data

An extract of the ClinicalTrials.gov clinical trial registry (obtained on 6 February 2017 through the clinicaltrials.gov download portal) was used for the analysis. 'Withdrawn' trials were excluded from the dataset as these trials did not actually enrol any participants.

The following key classifications were used to summarise clinical trial activity:

Phase: The records were classified into Phase I, Phase II (including Phase 1 / Phase 2 trials), Phase III (including Phase 2 / Phase 3 trials), Phase IV and Other (including those records that had no phase specified such as device trials).

Intervention type: The intervention type for each record was defined as Drug (all trials where 'drug' or 'biological' was an intervention type, excluding where 'device' was also an intervention type), Device (all trials where 'device' was an intervention type, excluding where 'drug' or 'biological' was also an intervention type) and Drug & Device (all trials where both 'drug' and / or 'biological' and 'device' were intervention types). 'Other' interventions included: 'behavioural', 'procedure', 'genetic', 'radiation', 'dietary supplement' (not exhaustive) and trials where no intervention type was specified.

Primary sponsorship type: The primary sponsorship type was classified into Industry (including 'Industry' and 'Commercial sector / Industry'), University, Individual, Government & Hospital (including 'Government body', 'NIH', U.S. Fed' and 'Hospital') and Other (including 'Other', 'Other Collaborative groups', 'Charities / Societies / Foundations' and trials where no sponsorship type was specified).

Global vs. local: 'Global' trials were defined as those that had recruitment in Australia in addition to one or more other countries. 'Local' trials were defined as those that had recruitment in Australia only.

Therapeutic area: TAs were determined using a search of key words within the 'conditions' field in the clinical trial database. Combined therapeutic areas included trials where key words for multiple therapeutic areas were found. The key word search methodology was based on the most frequently occurring words and supplemented by additional terms relevant to each therapeutic area.

World: Trials that were classified as 'World' excludes trials where no countries were specified for recruitment.

Appendix E. Analysis of ANZCTR data

i. Methodology

This report has leveraged an ANZCTR data extract, received on 10 February 2017 that was pre-filtered to all ANZCTR and ClinicalTrials.gov fed entries with recruitment in Australia. The analysis was based on the number of trials started per year, by 'actual start date'. Where trials had no 'actual start date' entered, the 'anticipated start date' was used. 'Withdrawn' trials were excluded from the dataset as these trials did not actually enrol any participants.

A relatively small number of the ClinicalTrial.gov records were duplicates of ANZCTR, indicating they had been entered into both registries. These duplicates were identified based on their linked unique IDs and were excluded from the dataset.

The classifications entered into the ANZCTR were grouped into the following segments to summarise clinical trial activity:

Phase: The records were classified into Phase I (including Phase 0 trials), Phase II (including Phase 1 / Phase 2 trials), Phase III (including Phase 2 / Phase 3 trials), Phase IV (including Phase 3 / Phase 4 trials), Device (including trials with only a device intervention type, however no phase was specified for device trials) and Other (including records that had no phase specified).

Intervention type: The intervention type for each record was defined as Drug (all trials where 'drug' or 'biological' was an intervention type, excluding where 'device' was also an intervention type), Device (all trials where 'device' was an intervention type, excluding where 'drug' or 'biological' was also an intervention type) and Drug & Device (all trials where both 'drug' and / or 'biological' and 'device' were intervention types). 'Other' intervention types included: 'behavioural', 'procedure', 'genetic', 'radiation', 'dietary supplement' (not exhaustive) and trials where no intervention type was specified.

Primary sponsorship type: The primary sponsorship type was classified into Industry (including 'Industry' and 'Commercial sector / Industry'), University, Individual, Government & Hospital (including 'Government body', 'NIH', U.S. Fed' and 'Hospital') and Other (including 'Other', 'Other Collaborative groups', 'Charities / Societies / Foundations' and trials where no sponsorship type was specified).

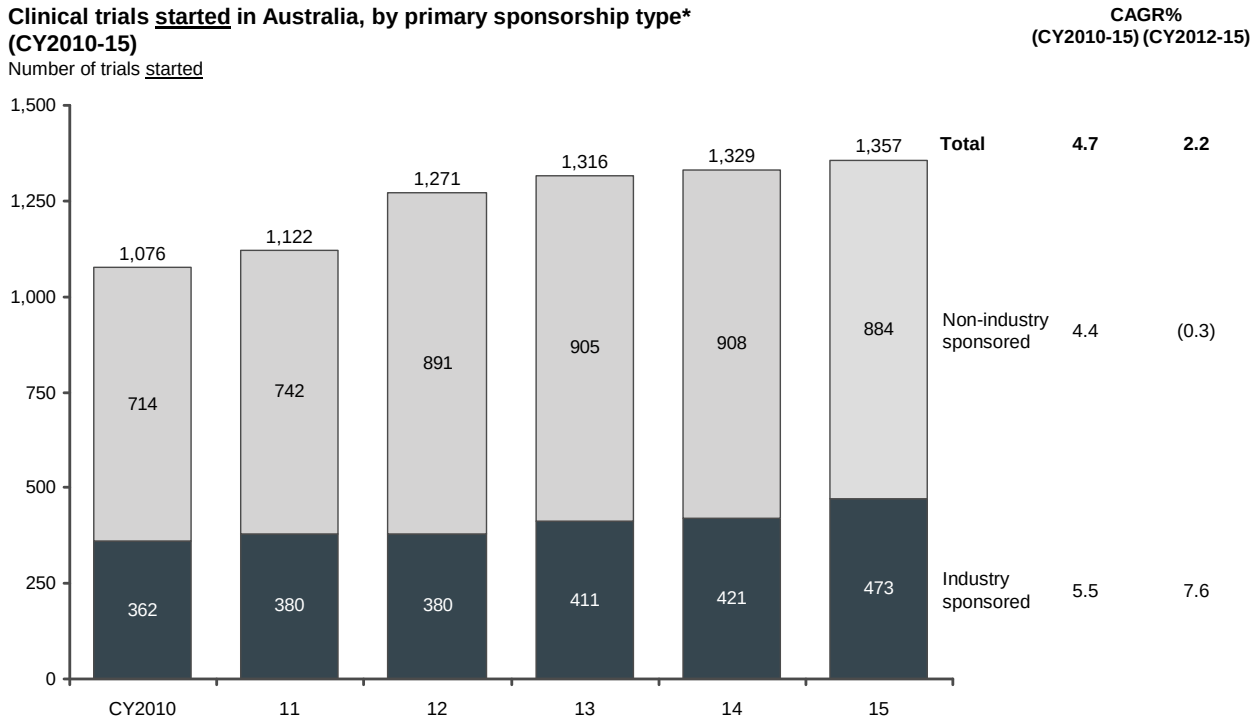
Funding type: Trials could be listed as having multiple funding types, either Industry (including 'Commercial sector / Industry'), Government & Hospital (including 'Government body', 'NIH', 'U.S. Fed' and 'Hospital'), University, Self-funded / Unfunded and Other (including 'Other', 'Other Collaborative groups', 'Charities / Societies / Foundations' and trials where no funding type was specified).

Global vs. local: 'Global' trials were defined as those that had recruitment in Australia in addition to one or more other countries. 'Local' trials were defined as those that had recruitment in Australia only.

ii. Additional analysis outputs

Notwithstanding data limitations, industry sponsored trials have grown at a greater rate than non-industry sponsored trial, particularly over the past three years.

Figure 23 Clinical trial starts in Australia, by primary sponsor

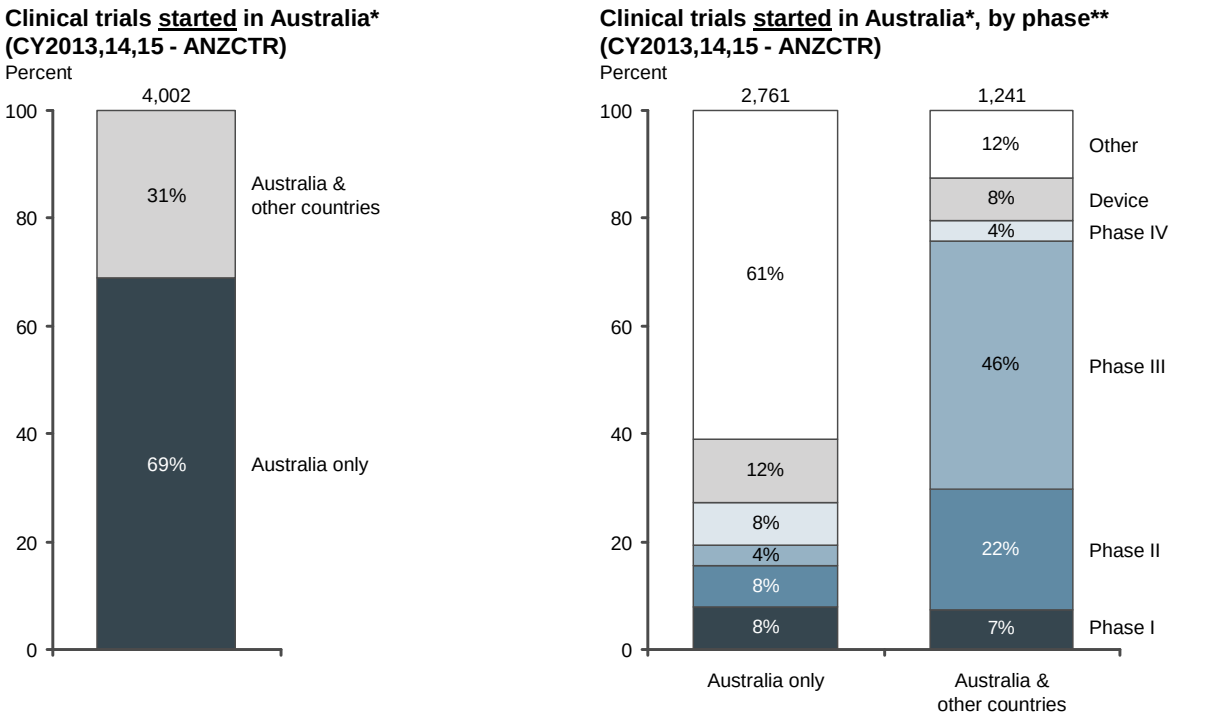


Note: * Excludes 'Withdrawn' trials and duplicate entries. Where trials had a 'NULL' actual start date, the anticipated start date was used. Industry sponsored includes: 'Industry' and 'Commercial sector/Industry'. Non-industry sponsored includes: 'Government body', 'NIH', 'U.S. Fed', 'Individual', 'University', 'Hospital', 'Other', 'Other Collaborative groups', 'Charities/Societies/Foundations' and trials where no sponsorship type was specified

Source: ANZCTR and ClinicalTrials.gov – combined by ANZCTR; L.E.K. analysis

Of the approximately 4,000 trials that were started between 2013 and 2015, approximately 69% were trials with local sites only. The remaining 31% of studies started in Australia were part of global multi-site trials. Global trials, i.e. trials with recruitment in Australia and elsewhere, are predominately Phase III trials.

Figure 24 Clinical trial starts, by location of trial sites



Note: * Excludes 'Withdrawn' trials and duplicate entries. Where trials had a 'NULL' actual start date, the anticipated start date was used. Global trials are those tagged in Australia and other countries. Local trials are those tagged in Australia only; ** Phase I includes 'Phase 0', Phase II includes 'Phase 1 / Phase 2', Phase III includes 'Phase 2 / Phase 3' and Phase IV includes 'Phase 3 / Phase 4'. 'Other' includes 'Not Applicable' or 'N/A', and trials with no phase indicated. Device includes all trials with a "Device" intervention type only – no breakdown of device trial phases is available

Source: ANZCTR and ClinicalTrials.gov – combined by ANZCTR; L.E.K. analysis

Appendix F. Analysis of TGA data

Due to the regulatory nature of the CTN scheme, the level of compliance of trial sponsors entering trial information is not considered an issue for TGA data in the same way as with voluntary registries. However, there are other challenges that need to be considered when using the CTN data set as an indicator of trial activity involving unregistered therapeutic goods in Australia. The primary purpose of the CTN data released by the TGA is to report on the activity levels of the regulator in assessing new applications. As a result, in instances where the regulator is required to perform multiple assessments for the same trial, this will be deliberately captured multiple times in the reported data since each assessment represents a new set of activity by the regulator. This "duplication" is a deliberate feature of the dataset since it primarily exists for activity reporting purposes. Instances in which multiple CTNs can be filed for the same trial, requiring multiple assessments, can include[111]:

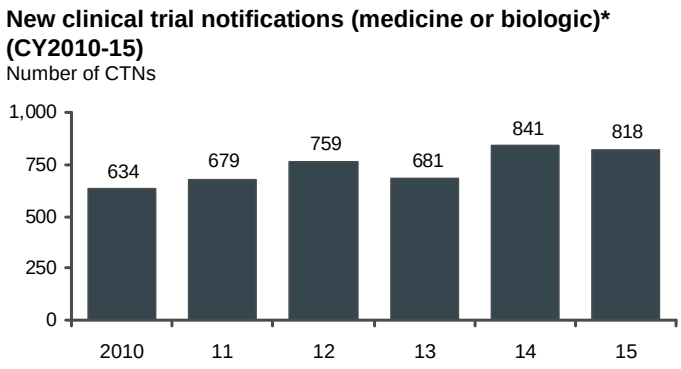
- international sponsors who appoint multiple CROs for the Australian sites of a trial. These CROs act as local sponsors and may submit separate CTNs
- a new CTN is required if there is a change in the therapeutic good, indication, or formulation of the product to be used in the trial and the product is not already approved for use in the relevant indication
- each hospital in a multi-centre trial may submit a separate CTN
- some sponsors may submit a new CTN for each different trial site and may not consistently consolidate to one submission after the fact

Many of these sources of duplication (e.g. related to multiple trial sites, or to minor changes to indication or formulation) have largely been eliminated with the introduction of the electronic Clinical Trial Notification (eCTN) system in 2015 which links together applications, better recognises amendments to existing applications and consolidates some assessment activity. However, it is currently not feasible to comprehensively assess the scale of duplication in CTN data. As a result, the growth rate and volume recorded in TGA data should be interpreted as directionally correct rather than precise, and it validates the findings of the ANZCTR analysis. The TGA have also indicated that a trend analysis across the years is not recommended since their form of capturing data changed with the introduction of the eCTN.

Historical CTN statistics suggest higher growth rates for medicines and device trials respectively than the ANZCTR. For the same period of 2010-2015, the data shows a compound annual growth rate of approximately 5.2% for clinical trials involving a medicine compared with 2.7% for the combined ANZCTR and clinicaltrials.gov activity data. However, due to changes in the data collection process during 2010 to 2015, data collected during this time period is not consistent across years, and as a result the growth rate is not considered accurate.

[111] This information has been obtained via L.E.K. and MTPConnect interviews with the TGA

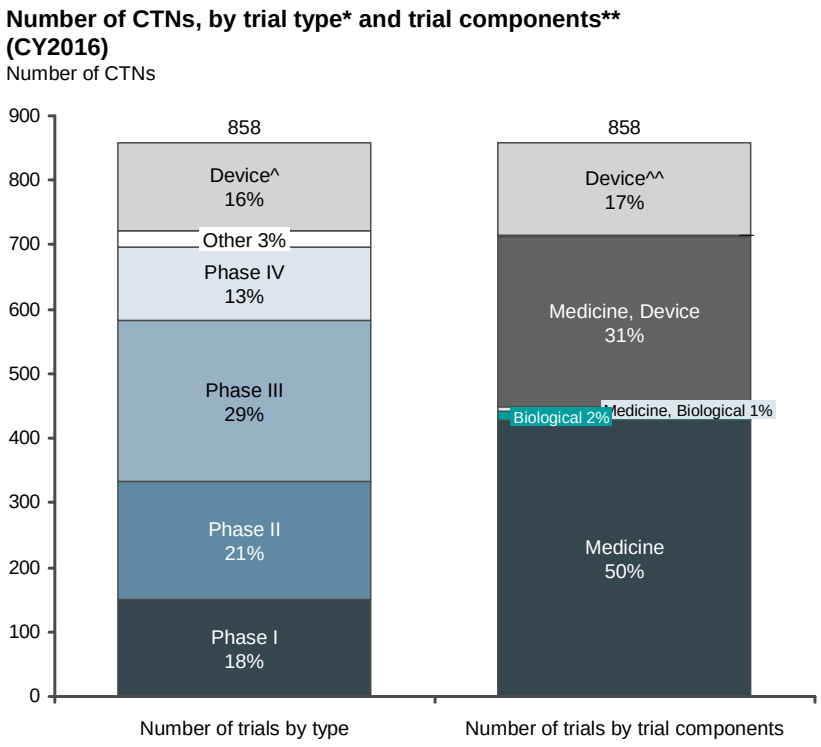
Figure 25 Clinical trial notifications - Medicine or Biologic



Note: * Medicine and biologic trials can also include devices
Source: TGA half yearly performance reports; L.E.K. analysis

For the purpose of this report, the TGA also supplied a requested extract of data from the eCTN system, however complete data was only available for 2016. Despite a considerable number of CTNs involving a medicine and a device, industry consultations suggest the majority of these notifications are for drug trials that also require an unregistered device in the conduct of the trial. The number of device trials in 2015 according to the ANZCTR dataset is very similar to the number of CTNs for trials that involve devices only in 2016.

Figure 26 Summary of CTNs by trial type and components - 2016



Notes: * Trial type as entered by the CTN applicant; ** Based on the flags selected by the CTN applicant to indicate that "this trial involves..", multiple flags can be selected for each trial; ^ Includes "Device", "Bioavailability/Bioequivalence, Device", "Phase 1, Device", "Phase 1, Phase 2, Device", "Phase 2, Phase 3, Device", "Phase 3, Device", "Phase 3, Phase 4, Device", "Phase 4, Device"; ^^ Trials involving only devices
Source: Special TGA data release; L.E.K. analysis

Appendix G. Estimation of the value derived from clinical trials – detailed methodologies

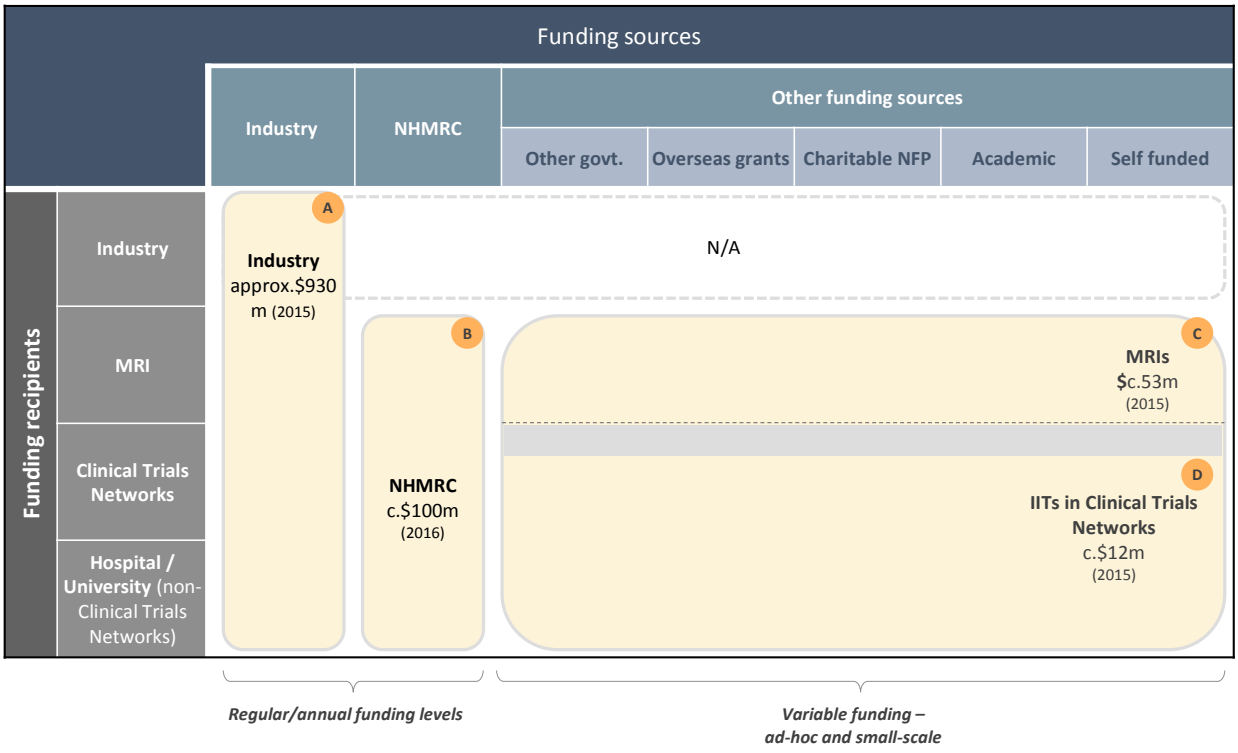
Availability and collection of economic data within the clinical trials sector is widely acknowledged to be limited. As a result, the calculations of the value delivered by clinical trials leverage a combination of existing data points and apply adjustment or scale factors to provide an estimate of the value of clinical trials in 2015.

i. Trial expenditure / funding

Total trial expenditure is the total money spent directly on the conduct of clinical trials within Australia. It includes private investment in clinical trials by MTP companies, grants and funding from the NHMRC, and a range of other funding contributed by various sources within the sector.

The total expenditure on trials was estimated through an approach that considered both sources of funding where they are aggregated (industry expenditure and NHMRC), and recipients that aggregate the majority of remaining funding sources (MRI trials and non-MRI IITs conducted through Clinical Trials Networks). This method may result in some marginal double counting between MRI expenditure and IITs within Clinical Trials Networks. This approach does not capture expenditure on or funding of IITs conducted outside of Clinical Trials Networks, however it is assumed that this is small compared to the entire sector expenditure.

Figure 27 Funding sources and recipients in the clinical trials sector



A – Industry expenditure

Industry expenditure on clinical trials has been calculated based on estimates released by the Pharmaceuticals Industry Council in 2011. In its report, the PIC surveyed 220 companies that were members of AusBiotech, MTAA, IVD Australia and MA, along with some additional CROs, to estimate total investment and employment in clinical trials. Of these, 104 were involved with some form of medical research in Australia and 53 completed the survey. While the headline response rate was 50%, it has been validated with the report's authors that the respondents represented the large majority of commercial expenditure in Australia. The report estimated that commercial investment in clinical trials in 2010 was approximately $607 million, including $12.4 million spent on IITs (this excludes $30 million for pre-clinical research).

To estimate the commercial expenditure in 2015, two adjustment factors have been applied to the 2010 expenditure figure reported by PIC:

- 2010 expenditure scaled up by the growth in the number of clinical trials from 2010 to 2015
- 2010 expenditure scaled up by inflation of 2.4% p.a. between 2010 and 2015 to reflect inflationary increases in average expenditure per trial

Table 19 Estimate of 2015 expenditure on clinical trials

	Spend on trials (2010, $m)	Number of trials (2010)	Number of trials (2015)	Change in trial volume	Inflation (PPTΔ 10-15)	Spend on trials (2015, $m)
Phase I	138	63	99	57%	12%	243
Phase II	92	93	112	20%	12%	124
Phase III	313	142	177	25%	12%	437
Phase IV	52	10	19	90%	12%	111
IIT	12	89	102	15%	12%	16
Total	**607**					**930**

The number of trials used to scale-up the 2010 expenditure were taken from the ANZCTR data extract detailed in Appendix E. with the following conditions applied:

- for Phase I – Phase IV, only trials where the primary sponsor was industry
- IITs included where they had industry funding (as determined by the investigator for ANZCTR), but where industry was not the primary sponsor
- all withdrawn trials were excluded from the analysis
- Phase I includes Phase 0, Phase II includes Phase I / II, Phase III includes Phase II / III and Phase IV includes Phase III / IV

As the PIC survey also included responses from CROs, it is possible that there is some double counting of expenditure reported by CROs that was also included by MTP companies. Due to a lack of availability of the underlying source data, it is not possible to determine the extent to which this has occurred.

Finally, it should also be noted that while the final figure of $930 million is incremental investment in the Australian economy, industry investment, and a portion of expenditure from other private sources, may be eligible for 38.5%-43.5% reimbursement from the government through the R&D tax incentive.[112]

B – NHMRC funding

The NHMRC provides funding for clinical trials both directly through project grants and indirectly through other grant schemes including fellowships, scholarships and infrastructure grants.

The NHMRC estimates that $100m is spent on clinical trials annually, with approximately $66 million[113] provided directly through project grants in 2016.

NHMRC funds are typically awarded to universities, MRIs or investigators (who utilise Clinical Trials Networks), they are not awarded to commercial companies.

Other Funding Sources

Other funding sources (outside of industry and NHMRC) are disparate and difficult to identify at the funding source. These funds have been estimated based on two points of aggregation in the sector through which a large amount of funding flows: MRIs and Clinical Trial Networks.

C – Other Funding Sources flowing through MRIs

Since neither AAMRI nor the individual MRIs track and publish clinical trial expenditure, an approximation method was leveraged for the purpose of this report. MRI expenditure on clinical trials was estimated by determining a proxy for the average percentage of MRI expenditure that is specifically for clinical trials, and applying it to the total MRI expenditure on clinical research, excluding revenue from industry or NHMRC that is already captured in A or B above. The proxy selected was the proportion of NHMRC funding that is provided to MRIs specifically for the purpose of clinical trials. Aggregate revenue and expenditure figures representing the majority of MRIs (38 independent MRIs from a total of 45 MRIs) were available from AAMRI, the industry association representing MRIs, through its 2016 Members Report.[114]

Figure 28 Calculation of MRI expenditure on clinical trials

The calculation includes the following steps:

i. Determine the portion of MRI research expenditure that is spent on clinical trials
   - the portion of NHMRC grants awarded to MRIs over the past 10 years that were for clinical trials was used as a proxy. L.E.K. analysis on the NHMRC grants database

[112] ATO identifies two incentives: a 43.5% refundable tax offset (for eligible entities with an aggregated turnover of less than $20m per annum) or a 38.5% non-refundable tax offset for all other eligible entities
[113] NHMRC - special data extract provided by NHMRC in 2017
[114] AAMRI, Members Report, 2016

indicates that **10.4%** of all grants awarded between 2006-15 to MRIs were for clinical trials

ii. Calculate MRI expenditure on medical research excluding commercial expenditure and NHMRC grants

- approximately 59% of total MRI revenue in 2014 was spent on research
- MRI revenue excluding commercial income and NHMRC grants was $843 million in 2014
- therefore, it is estimated that $498 million of non-commercial / non-NHMRC revenue was spent on medical research in 2014, or **approximately $507 million** in 2015 assuming 2% growth as reported by AAMRI

iii. Calculate the implied expenditure on clinical trials by MRIs

- 10.4% of $507 million equates to **approximately $53 million** in 2015

This method assumes that the average percentage of NHMRC grants that are for clinical trials is representative of the total percentage of MRI revenue that is spent on clinical trials. While this is unlikely to be the case for all MRIs, it is also recognised that not all MRIs are conducting clinical trials. It is thus assumed that the percentage identified through the proxy is the floor for expenditure. Double counting has been avoided by excluding revenue from MTP companies and NHMRC as it is captured in A and B above. The result may further understate the total expenditure on clinical trials by MRIs as the aggregate figures reported by AAMRI do not include non-independent MRIs, and so their expenditure on clinical trials is not counted. Funding can flow through a variety of sources, such as universities, which are not captured by MRIs.

D – Other Funding Sources flowing through Clinical Trials Networks

The final component of clinical trial expenditure that has been quantified results from IITs that are typically conducted within Clinical Trials Networks in collaboration with hospitals and universities.

The majority of IITs (excluding those conducted in MRIs) are assumed to be conducted with some association to Clinical Trials Networks, and therefore funding for these trials has been estimated using the ACTA's evaluation of investigator-initiated clinical trials conducted by networks (2017).[115] This report tracks expenditure flowing through Clinical Trials Networks to MRIs, universities and other coordinating units.

The ACTA report contains an estimate of the total funding received for a sample of clinical trials undertaken by Clinical Trials Networks that were current as of 31 December 2014, regardless of commencement date. It was developed based on detailed data collection in a survey from member networks. The sources of funding for IITs within Clinical Trials Networks include:

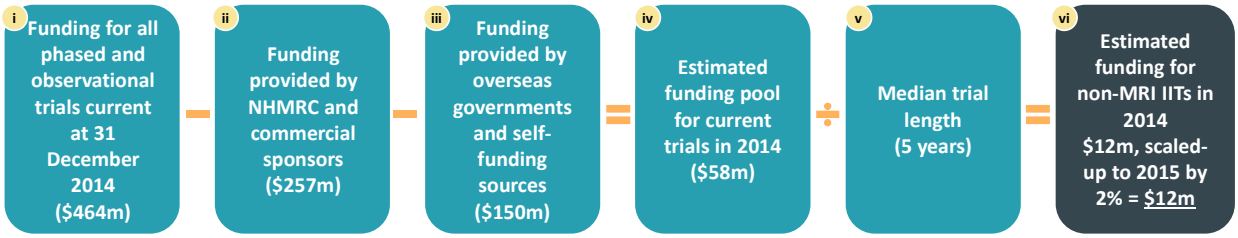
- NHMRC

[115] A recent perspective on the impact of implementing a subset of clinical trials can be found in Australian Clinical Trials Alliance, Economic evaluation of investigator-initiated clinical trials conducted by networks, 2017 (based on an analysis of 25 high impact clinical trials)

- other government (including overseas governments)
- charitable / not-for-profit
- commercial / industry
- local hospitals
- self-funded and academic

By excluding funding sources that are already captured in methods above (e.g. NHMRC and commercial), the resulting funding amount can be considered as additional expenditure on IITs within Clinical Trials Networks. A number of steps were required to obtain this figure:

Figure 29 Calculation of non-MRI expenditure on IIT clinical trials



i. The ACTA analysis collected details of funding on a sub-set of clinical trials that were conducted by Clinical Trials Networks and current as of 31 December 2014. For Phase I-IV and observational trials, funding amounted to approximately $464m

ii. Funding from NHMRC ($208m) and commercial sponsors ($49m) was excluded, as these sources are already captured in A and B above

iii. Funding from overseas governments ($125m) is also excluded, as it largely applies to trials with patients outside Australia. Similarly, a range of self-funding sources ($24m) are excluded. Self-funding sources often provide in-kind value rather financial investment

iv. With the above funding sources excluded, a funding pool of $58m remained for all current trials in 2014

v. The $58m figure accounts for spend throughout the duration of the trials tracked by ACTA and must be divided by the median trial length to estimate the funding for non-MRI IITs in a single year. For the purposes of its analysis, ACTA defined trial length as the time between receipt of NHMRC funding and publication of results. Median trial length was calculated as 5 years for NHMRC funded trials and this was assumed to be indicative of all trials in the study

vi. By dividing $58m by 5, L.E.K. estimates that $12m was spent on non-MRI IITs in 2014. Assuming the same funding growth of 2% per annum that was assumed for MRIs, this equated to **approximately $12m** in 2015

ii. Employment

For the purposes of this report, employment within the clinical trial sector is considered in two distinct segments:

1. Research and management jobs supported at MTP companies or service providers such as CROs - **estimated to be 4,700**
2. Clinical staff supported within hospitals, clinics or other trial sites – **estimated at 2,200**

Research and management staff

A study completed by the Pharmaceuticals Industry Council R&D Task Force in 2009 identified that there were approximately 3,400 jobs supported within industry (including at MTP companies and at CROs).[116] This estimate was based on data held by ARCS Australia. Although some large MTP companies have noted a decline in local clinical trial operations (and hence employment) it is likely that they have increased their use of outsourced expertise through CROs. Under the assumption that total research and management staff employed increase in line with the growth in industry sponsored trials, it is estimated that there are **4,700** jobs supported by clinical trials in 2015.

Figure 30 Estimation of research and management jobs supported by trials in 2015

Clinical staff

The number of clinical staff supported by clinical trials is difficult to estimate due to the often part-time nature of clinical trial roles and the lack of available data for employment within the healthcare system in Australia.

The number of clinical staff supported by trials has been estimated on the basis of a survey of clinical trial investigators, published by the PIC in 2009. Based on the participants of this survey, it was estimated that there were 1,718 investigators, co-investigators, research nurses, study coordinators and data managers in Australia at the time. This was reported as a headcount figure and may include double counting due to the anonymised nature of the report.

The number of clinical staff supported by trials in 2015 has been estimated to be **2,200,** assuming the same yearly growth as total clinical trial starts between 2010 and 2015. This figure was sense-checked through discussions with clinical trial units at a number of hospitals and local health areas / districts in Australia.

Figure 31 Estimation of clinical staff supported by trials in 2015

[116] Pharmaceuticals Industry Council, Assessing the Value of Industry Sponsored Clinical Trials, 2009

iii. Growth outlook

The growth outlook for the clinical trials sector by 2025 has been quantified under two growth scenarios (low case and high case).

Growth in trial expenditure is likely to come from both an increase in the number of trials and an increase in the number of participants per trial. As outlined below, expenditure is first grown by considering an increase in total trial volumes. Secondly, expenditure is grown to take account of potential increases in patients per trial by assuming a variable cost proportion of 75%. As the number of patients per trial is increased, not all costs will increase in proportion to the number of patients – it has been estimated that 75% of costs will increase in line with additional patients. The other 25% of costs are considered fixed (i.e. not effected by increasing the number of participants per trial).

Figure 32 Calculation of sector expenditure for growth scenarios

Two scenarios have been developed – a low case and a high case.

- the low case assumes that the observed historical growth rate in total trial starts (from 2010-15) will continue for the next 10 years and average number of patients per trial will increase by 25% by 2025
- the high case assumes more aggressive growth for both trial volumes and number of participants per trial, as outlined in the table below
- both scenarios assume 2.7% inflation p.a., based on the Oxford Economics Forecast Databank

Table 20 Growth scenario assumptions

Assumption		Value	
		Low case	High case
Growth in industry trial volumes	X%	4.7% p.a.	6.7% p.a.
Variable portion of expenditure		75%	75%
Growth in patient numbers	Y%	25% (by 2025)	50% (by 2025)

Table 21 Growth scenario expenditure

	2015 ($m)	2025 scenarios	
		Low case ($m)	High case ($m)
Expenditure	1,095	2,080	2,530

The expenditure in the sector by 2025 is approximately $2.1 billion in the low case, and approximately $2.5 billion in the high case.

Similarly, total sector employment was estimated for a high and low case. Employment growth was assumed to mirror the growth in expenditure, minus inflation. This is a simplifying assumption, given that the number of FTEs aligned to clinical trials is not expected to grow in line with total expenditure. The number of FTEs required to conduct a clinical trial are not uniformly allocated, and an increase in trial activity does not necessarily result in a 1:1 increase in FTEs. Some roles increase in line with the number of trials, while others increase in line with the numbers of patients, number of sites or complexity of trial design. As data coverage of clinical trials employment improves, more accurate forecasting methodologies should be utilised.

Figure 33 Calculation of employment for growth scenarios

Table 22 Growth scenario employment

	2015	2025 scenarios	
		Low case	High case
Employment	6,900	12,900	15,600

The employment in the sector by 2025 is approximately 13,000 in the low case, and approximately 16,000 in the high case.

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