A ustralia has a long and distinguished history in medical research, with many medical breakthroughs and their associated intellectual property originating from Australian scientists. Australian Nobel laureates in medical research span discoveries such as penicillin, key developments in immunology, through to the bacterial causation of gastric ulceration. This focus on medical research has produced an environment that is strongly supportive of clinical research at the public, institutional and government level. Until recently Australia has been known for its participation in later phase trials. However Australia has now become just as well known for its early phase (I-IIa) clinical trial work.

Australia has a strong reputation for the quality of its medical and scientific research. Importantly in relation to Good Clinical Practice, the Australian pharmaceutical regulator the Therapeutic Goods Administration (TGA) has adopted the European Guideline CPMP/ICH/135/95 (and hence the ICH E6 guidance) in principle, with annotations according to local regulatory requirements. Adherence to ICH GCP is, under Regulation 12AB of the Therapeutic Goods Regulations 1990, and is mandatory in Australia for all clinical trials. In 1991, the TGA introduced the
Clinical Trial Notification (CTN) scheme. This scheme allows clinical trials of unapproved medicinal products and devices to be conducted without the need for regulatory review and approval by the TGA. Previously in Australia, all trials required a regulatory review, similar to the UK’s CTX (Clinical Trial Exemption) guidelines. The Australian CTX process requires 50 working days review time and concurrently requires an institutional ethics committee approval (following CTX approval).

The CTN system requires an institutional ethics committee approval which covers both the ethical and scientific review. Ethics committees in Australia generally meet on a monthly basis. Therefore it is possible to obtain Ethics approval within 30 days following submission and then lodge a notification (CTN) to the TGA, with acknowledgement being received within 7 days. The introduction of the CTN system to Australia has resulted in strong growth in the number of trials undertaken in Australia, with around 2,500 CTNs (multiple site) lodged in 2005. A concomitant decrease in CTX applications has also resulted (three in 2005). This increase in clinical trial work has strengthened documentation quality and has not in any way compromised the safety of trial volunteers.

With the implementation of the CTN scheme and the European Union Directive on clinical trials, the early phase (I-IIa) sector has become the fastest growing area of clinical trial activity in the country. The majority of phase I and proof-of-concept studies can be conducted under the CTN scheme without the burden of an EU CTA or U.S. IND, a significant advantage in the extremely time critical development pathway. Notably this includes first time in human studies of monoclonal antibodies and other biologics. The data, generated to ICH GCP standards and subject to stringent IP laws, can be used to enhance capital raising, partnership discussions and to support planned clinical trial applications in the European Union and the United States at a later date.

Australia is known as a high quality and relatively low cost destination for clinical trials. However there is a lack of publicly available data on the nature and number of clinical studies conducted in Australia, particularly in recent years. What data are available are generally kept in-house within the pharmaceutical and biotechnology companies’ walls.

In 2005 an international benchmarking study was undertaken by The Economist Intelligence Unit which reported Australia as the number one location to conduct pharmaceutical clinical trials. The Economist Intelligence Unit study, “Benchmarking Study of the Australian and International Pharmaceuticals Industries,” was commissioned by the Australian Government Department of Industry, Tourism and Resources; Invest Australia; and the Victorian Government Department of Innovation, Industry and Regional Development (Full report available at: www.industry.gov.au). It benchmarked Australia against the United States, the United Kingdom, Germany, Japan, Singapore, and India across the industry as a whole with indicators such as clinical trials, intellectual property, the regulatory environment, and the investment and business environment.
Australia was ranked first for clinical trials due to three main factors:
- Low average cost of clinical trials
- Large number of recognised trial sites
- High percentage of clinical trials completed on time.
Interestingly, Australia was ranked relatively low in terms of the numbers of trials conducted per capita of population. This presents an opportunity to utilise the additional capacity to undertake clinical trials in Australia.

Currently, there are a number of initiatives to support the clinical trial industry in Australia:

1. Joint regulatory harmonisation between New Zealand and Australia to streamline submissions for obtaining clinical trial approval under the Australia New Zealand Therapeutic Products Agency (ANZTPA). At this stage of the harmonisation process, it is planned that ANZTPA will retain the current CTN/CTX system for access to unapproved therapeutic goods. However, elements of the two separate systems may be retained in accordance with local requirements.

2. Government backed multi-center ethics review projects, to reduce the number of ethics submissions required for multi-centre studies.

3. Simplification to a National Ethics Application Form (NEAF)

4. Industry agreed standard indemnity wording (Medicines Australia Form of Indemnity for Clinical Trials)

5. Industry agreed standard Clinical Trial Agreement

6. Establishment of Australian chapter of Association of Clinical Research Professionals by Nucleus Network

There are also a number of portals into the Australian industry. Examples include Nucleus Network (Centre for Clinical Studies, Clinical Trials Consulting and Nucleus Network Education) and the Australian and New Zealand Biotechnology Alliance (ANZBA).
Conducting Clinical Trials in Australia

The Australian Health Care System has a mix of public and private sector providers delivering health services. The quality of health care provided is high in both sectors and is supported by a federal health system. This system aims to give universal access to health care while allowing choice for individuals through the private sector. Hospitals in both the private and public sectors are committed to medical research and are the source of experienced clinical trial sites with GCP trained investigators and staff.

The following topics summarise the processes involved in conducting clinical trials in Australia:

1. Australian Government Bodies overseeing clinical trials
2. Regulatory approval to conduct clinical trials
3. Ethics Approval and Ethics Approval Timelines
4. Informed Consent
5. Access to healthy volunteers and patients, and Patient Recruitment Issues
6. Indemnity and Insurance
7. Clinical Trials materials
8. Study close-out and archiving

1. Australian Government Bodies Overseeing Clinical Trials

There are two major Australian Government bodies

- Therapeutics Goods Administration (TGA). The TGA acts as Australia’s regulatory authority in relation to the registration and/or listing of medicinal products including medical devices. The TGA has adopted ICH GCP in principal with minor annotations for specific local requirements. Clinical trial data generated in Australia are acceptable to the FDA and EMEA subject to review.

- The National Health and Medical Research Council (NH&MRC). The NH&MRC allocates funds for health and medical research, provides health advice, and regulates the requirements of the ethics committees and sensitive medical research activities.

- It is important to note that clinical trials involving gene therapy or related therapies require approval from both the HREC and the Gene and Related Therapies Research Advisory Panel (GTRAP), an expert committee established by the NHMRC.
2. Regulatory Approval to Conduct Clinical Trials

Australian Legal Entity
The sponsor of a clinical trial in Australia must be an Australian corporate entity.

Several local and international Clinical Research Organisations (CROs) can make arrangements to act as the Australian sponsor of a clinical trial if the overseas sponsor does not have an Australian affiliate to fulfil this role.

Australian Regulatory System
As discussed there are two routes that may be taken to gain regulatory approval to conduct a trial — the Clinical Trial Exemption (CTX) and Clinical Trial Notification (CTN) schemes.

Summary of Australian Regulatory Process

<table>
<thead>
<tr>
<th>Process</th>
<th>CTN (Clinical Trial Notification)</th>
<th>CTX (Clinical Trial Exemption)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGA Review</td>
<td>Not required</td>
<td>√</td>
</tr>
<tr>
<td>HREC Approval</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Agency Timelines</td>
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<td>30 days or 50 days</td>
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<td>Fees</td>
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<td>$A15,300 ($US11,964)</td>
</tr>
<tr>
<td>% per year</td>
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<td>1</td>
</tr>
</tbody>
</table>

These two schemes are used for clinical trials involving:

- any product not entered on the Australian Register of Therapeutic Goods; or
- use of a registered or listed product in a clinical trial beyond the conditions of its marketing approval.

Clinical trials with registered or listed medicines or medical devices used within the conditions of their marketing approval are not subject to CTN or CTX requirements. However, they still need to be approved by a Human Research Ethics Committee (HREC) before the trial may commence.
3. Ethics Approval and Ethics Approval Times

Human Research Ethics Committees (HRECs)

Irrespective of route, CTN or CTX, all clinical trials must be submitted to an Australian, independent, HREC. HREC must comply with the requirements of the NH&MRC which has a responsibility to oversee their operation. Most HRECs meet on a monthly cycle.

The submission must be comprised of, but not limited to the following:

- Study protocol
- Investigational Brochure (IB) drug and/or device
- Patient Information & Consent Form
- Completed ethics application form
- Clinical Trial Agreement
- Clinical Trial Insurance Certificate
- Site indemnities (Medicines Australia Form of Indemnity for Clinical Trials)
- Advertising materials or information provided to subjects
- Regulatory Form (CTN or CTX)

4. Informed Consent Forms (ICF)

Sites are required to have their own participant information and consent forms that comply with:

- NH&MRC Guidelines
- Individual HREC guidelines
- ICH GCP

Sites are required to produce their own participant information and consent forms that comply with the individual HREC’s requirements (template), NH&MRC guidelines and ICH GCP. The local requirements in combination with ICH generally satisfy the requirements of Code of Federal Regulations (21 CFR Part 50 and 56 in the USA). Australian details on data protection, patient compensation, reimbursement, contact details for an emergency as well as independent advice must be provided.

5. Access to Healthy Volunteers and Patients and Patient Recruitment Issues

Many of the clinical trial units in Australia are in close proximity to major teaching hospitals, universities and academic institutions. This provides Sponsors access to healthy volunteers and to patient populations in numerous therapeutic areas. Australia’s multiculturalism also provides access to varied ethnics groups in a concentrated demographic area.
6. Indemnity and Insurance

The Australian Sponsor must provide site indemnities as part of the ethics submission in the form of Medicines Australia Form of Indemnity for Clinical Trials (www.medicinesaustralia.com.au). The wording on the indemnity is accepted nationwide and should not be altered.

Clinical trials insurance is required to be held by the Sponsor for the duration of the clinical trial. Some Australian states have specific requirements regarding the level of insurance cover and the deductible if any. A copy of the sponsor’s certificate of insurance is required as part of the ethics submission.

7. Clinical trials Materials

Australia is a beautiful island and very protective of its borders. However in general a specific clinical trial import permit is not required for clinical trial material. However some clinical trial materials may be subject to additional restrictions and separate approvals may be required (for example, products containing substances that are listed as prohibited imports, and materials of biological origin).

Local temperatures can exceed 36°C during summer months and safe storage of materials is very important and should be supported by appropriate stability information.

Drug or Device Labelling Requirements

As the majority of clinical trials are blinded, there is a need to ensure that contents of clinical trials packaging are easily and rapidly identifiable and appropriate labelled. Furthermore, in Australia, there is a requirement for an expiry date to be included on the label of the packaging. This expiry date needs to be supported by stability data.

More information on labelling requirements can be sought from www.tga.gov.au/docs/pdfl/unapproved/unapp.pdf

8. Study Close-out and Archiving

Australian regulations stipulate records be retained for at least 15 years following completion of a clinical trial. Investigational sites often request additional financial support from the sponsor for off site archiving by a third party or that the sponsor supports this process directly. All other study close out activities are in accordance with ICH GCP requirements.

The combination of quality medical and scientific research and high quality, cost effective clinical trials makes Australia a compelling destination for drug development. I invite you to consider Australia for your next clinical trial!
References


2. Therapeutic Goods Act 1989, Commonwealth of Australia

3. Therapeutic Goods Regulations 1989, Commonwealth of Australia


5. Australia New Zealand Therapeutic Products Authority Treaty, 2003