NOVOTECH
The Asia Pacific CRO

Regulatory requirements for clinical trials.

A comparison of Australia and the US.

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Introduction and Executive Summary

With a streamlined regulatory environment, including no requirement for an IND, and the supportive R&D Government refund of up to 43.5% on clinical research spend, Australia has become a preferred destination for early phase clinical trials. The number of clinical trials has grown solidly in the last few years in Australia, enjoying over 10% growth per annum between 2016 and 2018.

The rapid Australian and New Zealand regulatory and ethics (equivalent to IRB) processes often means biotechnology companies can initiate their clinical programs and commence dosing within a single review cycle of 6-8 weeks from submission. As a result, many biotechnology companies can commence a clinical trial in parallel to the preparation of a US IND submission.

This report aims at highlighting the benefit of running clinical trials in Australia and to compare the regulatory requirements of Australia and the US.

1. Landscape of early phase clinical trials in Australia

The regulatory environment in Australia and New Zealand offers a significant strategic opportunity for international biotech companies wanting a fast and pragmatic regulatory pathway for early phase clinical trials.

With streamlined regulatory requirements, including no requirement for an IND, and the supportive R&D Government refund of up to 43.5% on clinical research spend, Australia has become a preferred destination for early phase clinical trials.

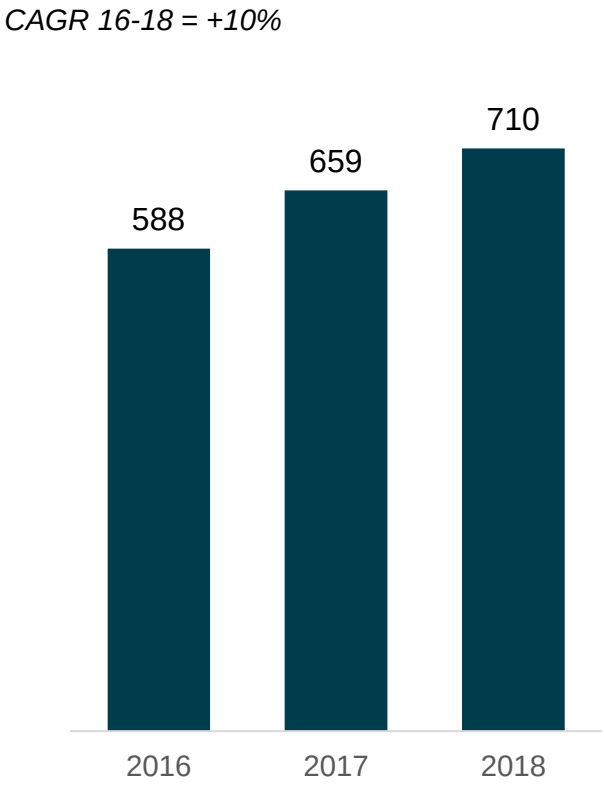
Importantly Australia and New Zealand also offer alternative recruitment potential to northern hemisphere seasonal related studies.

The number of clinical trials has grown solidly in the last few years in Australia, enjoying over 10% growth per annum between 2016 and 2018 (graph 1).

While the simplified regulatory framework, and the cash refund scheme has brought many biotechnology companies to Australia for their first-in-human trials, the phase mix remains balanced over that period (graph 2) with a significant portion of late phase trials also.

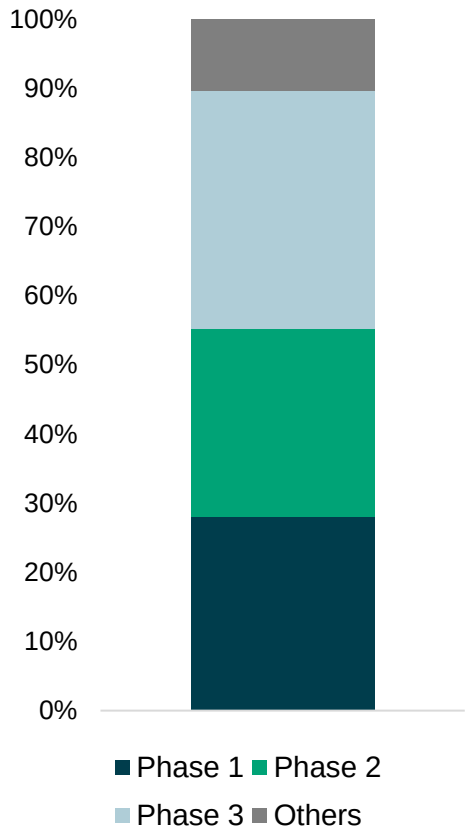
Graph 1. Number of clinical trials initiated in Australia each year (2016 – 2018)

Source GlobalData



Graph 2. Breakdown of studies initiated in Australia (2016-2018) by phase.

Source GlobalData



2. Regulatory process and requirements

The Therapeutics Good Administration (TGA) is the regulatory body in Australia and has adopted European Union (EU) and ICH quality, nonclinical and clinical guidelines. To conduct a clinical trial in Australia, the trial must have an Australian Sponsor. There are two major systems for submission of a clinical trial protocol, the clinical Trial Notification (CTN) or the Clinical Trial Exemption (CTX) scheme. The CTN scheme provides notification to the TGA of conduct of a clinical trial that has been reviewed and approved by a Human Research Ethics Committee (HREC). The TGA is not involved in review of the nonclinical data under this scheme. The CTX scheme is less frequently used and is for higher risk or novel treatments such as some cellular or gene therapies where there may be limited knowledge of their safety. A CTX scheme is mandatory for Class 4 biologicals.

A US Investigational New Drug (IND) submission is not necessary to initiate first-in-human clinical trials in Australia. FIH trials in Australia are of high quality and are acceptable to other regulatory agencies in support of later Phase clinical trials. The simplicity and efficiency of the Australian and New Zealand regulatory and ethics processes often means biotechnology companies can initiate a clinical trial in parallel to the preparation of a US IND submission, often commencing dosing within a single review cycle of 6-8 weeks from submission.

Figure 1. Site start-up timelines (public and private sites) in Australia (CTN scheme)

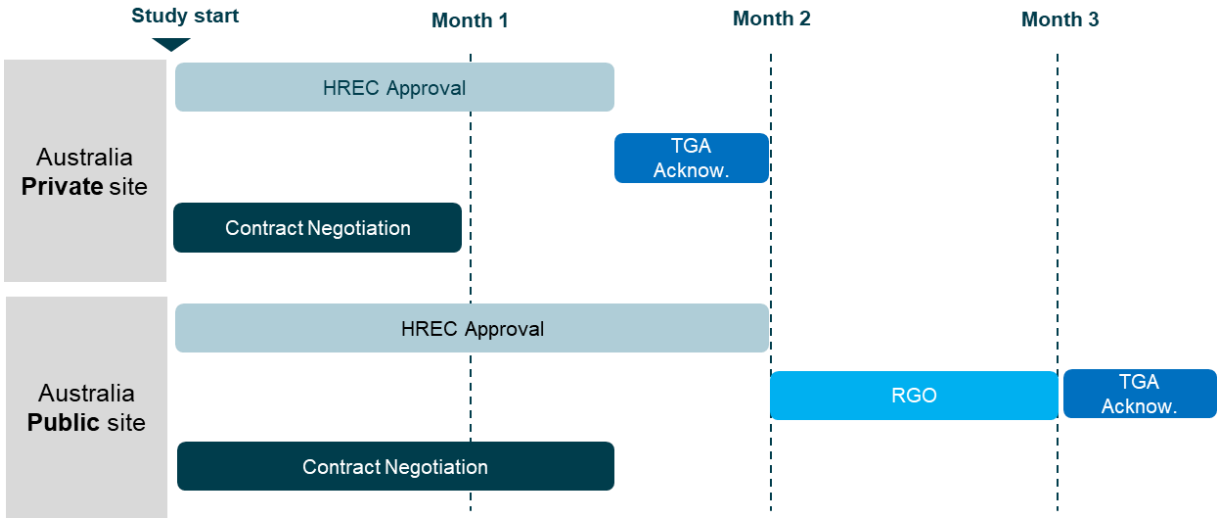


Figure 2. Timeline estimates for a first-in-human completion in Australia compared with Europe and North America

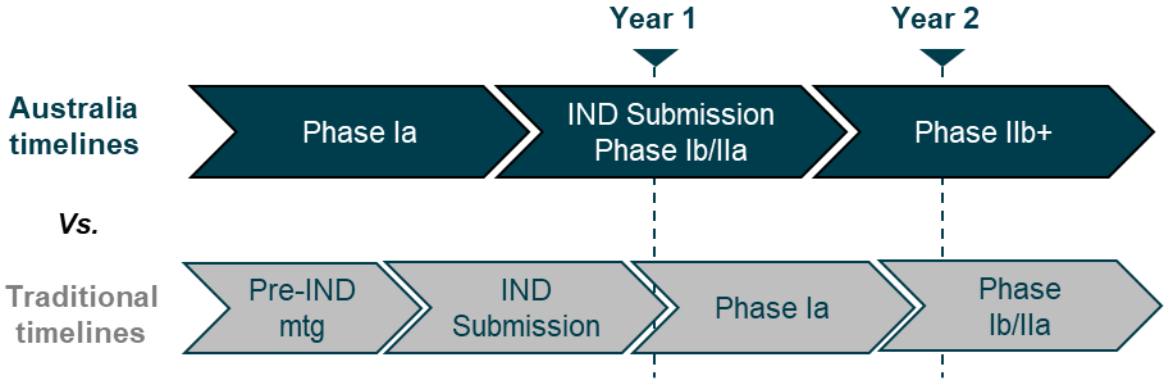


Table 1. Clinical trial application requirements in Australia, US and EU

Australia	EU	US
CTN (majority of applications) or CTX	Full CTA to the national competent authority in the Concerned Member State	A full IND is required to be submitted by the investigator before a clinical trial can be initiated

• Overview of key documentation: IB/Protocol/Informed consent form/Patient information
• Resource burden: CTN – Low; CTX – Moderate
• Timeline for document preparation:
  ○ CTN: 1-1.5 month
  ○ CTX: 2–3 months
	• Overview of key documentation: IB/Protocol/IMPD/Informed consent form/Patient information
	• Resource burden: Moderate
	• Timeline for document preparation: 2–3 months
		• Overview of key documentation: IB/Protocol/IND/Informed consent form/Patient information
		• Resource burden: Moderate
		• Timeline for document preparation: 2–3 months

The TGA recommends HREC in Australia to consider the EU and ICH guidelines on non-clinical studies when reviewing protocols.

Key non-clinical requirements warranted for first-in-human trials are dependent on the scope of the clinical trial and the type of product being developed. As an example, the following information would be expected for a typical oral or intravenous new chemical entity:

- In-vitro metabolic and plasma protein binding data.
- Pharmacokinetic information to support the dose route and dose regimen intended to be used clinically.
- Repeated dose toxicity studies typically in two species (one non-rodent) are needed to support any clinical development trial (Table 2). If only one species are used this should be scientifically justified.
- An assay for gene mutation is generally considered sufficient to support a single dose clinical development trial. To support multiple dose clinical development trials, an additional assessment capable of detecting chromosomal damage in a mammalian system should be completed.
- Safety pharmacology data.
- Reproduction toxicity studies are not typically required for a Phase 1 trial as long as acceptable contraception and pregnancy testing are incorporated in the clinical trial protocol.
- Other toxicity studies may be required depending on IP profile and route of administration used.

ICH M3(R2) details the minimum repeat dose durations for toxicity studies (Table 2)

Table 2. Recommended Duration of Repeated-Dose Toxicity Studies to Support the Conduct of Clinical Trials

Maximum Duration of Clinical Trial	Recommended Minimum Duration of Repeated-Dose Toxicity Studies to Support Clinical Trials	
	Rodents	*Non-rodents*
Up to 2 weeks	2 weeks	2 weeks
2 weeks to 6 months	Same as clinical trial	
Over 6 months	6 months	9 months

Table 3. Main documents required for regulatory and ethics committee submissions
Source: clinregs.niaid.nih.gov [accessed 11th February 2020]

Document	AUS	USA
IND required		X
Final Protocol	X	X
In-country sponsor representation required	X	
Investigator brochure	X	X
GMP Cert (Manufacturer)		X
Certificate of Analysis		Suggested
ICF	X	X
Patient facing documents	X	X
Recruitment procedures	X	X
Investigator CVs	X	X
SAE form		X
Patient ID Card	X	
Insurance certificate	X	X
Clinical trial registration	X [a]	X [b]

[a] *Any WHO-recognized registry is acceptable (such ANZCTR)*

[b] *ClinicalTrials.gov databank is required*

Let's continue the discussion

Novotech provides regulatory and clinical consulting services to biotechnology companies through its specialized division BioDesk.

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