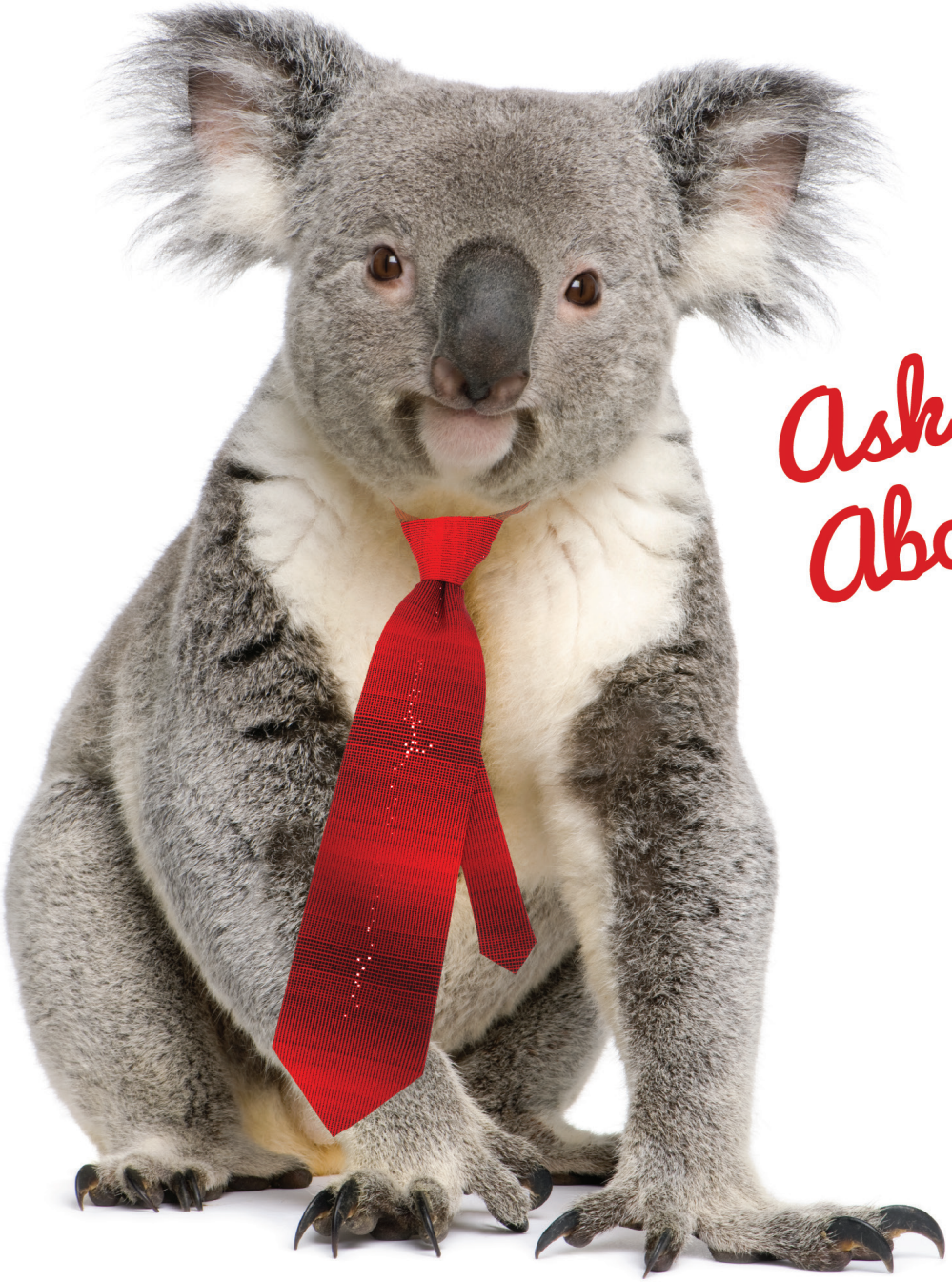
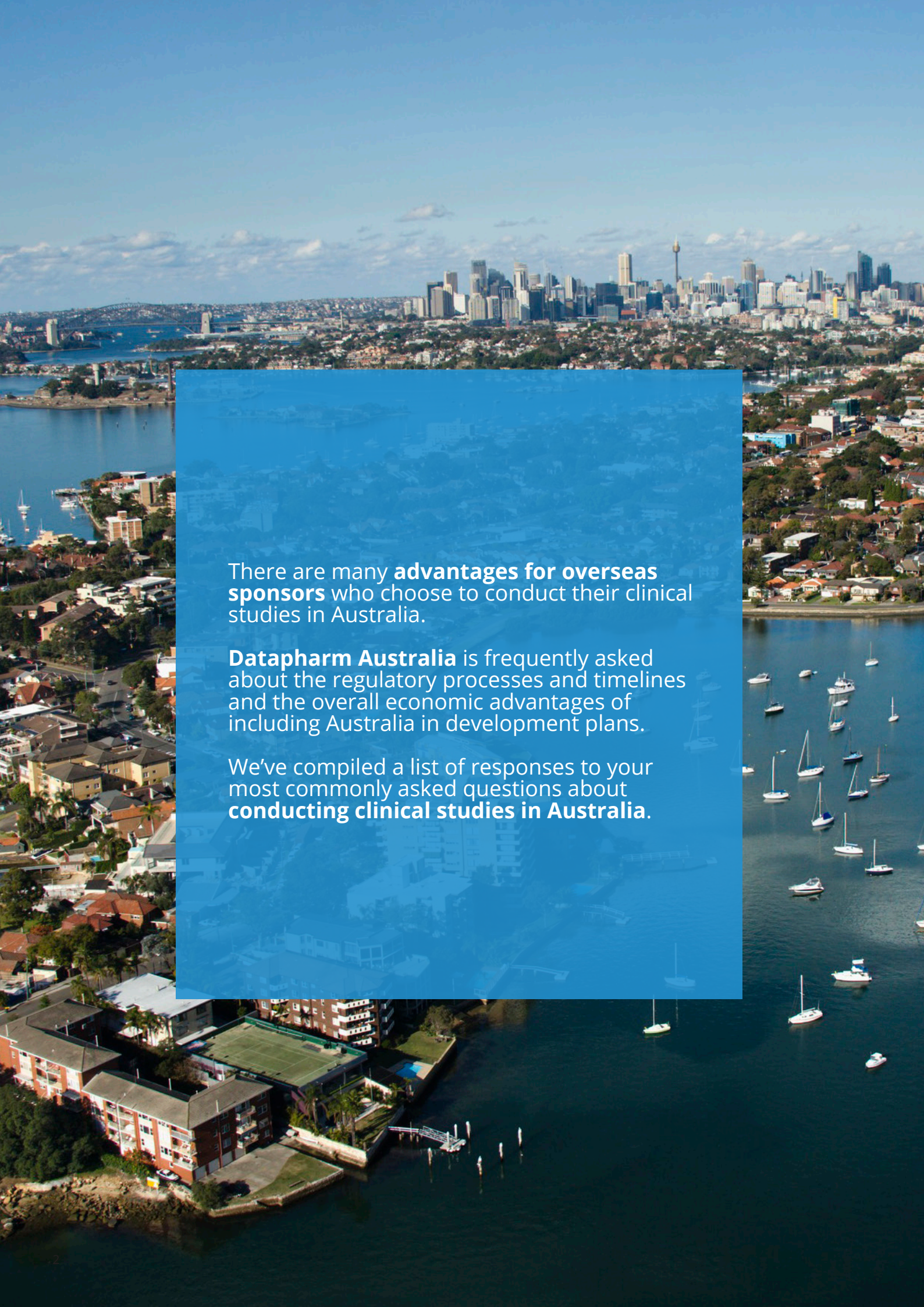


Practical Guide to Extending Clinical Trials to Australia

Australian CLINICAL TRIALS



There are many **advantages for overseas sponsors** who choose to conduct their clinical studies in Australia.

Datapharm Australia is frequently asked about the regulatory processes and timelines and the overall economic advantages of including Australia in development plans.

We've compiled a list of responses to your most commonly asked questions about **conducting clinical studies in Australia**.

Can an Overseas Company Sponsor Clinical Trials in Australia?

SPONSOR LEGAL ENTITY

The sponsor of a clinical trial in Australia must be a legal entity in Australia. It is simple to register this legal entity with TGA (Therapeutic Goods Administration) by obtaining an 'Organisation Details ID' using the following form: www.tga.gov.au/form/organisation-details. [Note this replaces the earlier 'Client ID']. The legal entity can also obtain online access to TGA Business Services (TBS): www.tga.gov.au/tga-business-services-getting-started-tga.

HOW TO CREATE THE LEGAL ENTITY

The approach of some overseas companies, is to ask their chosen CRO (Contract Research Organisation) to act as their sponsor in Australia. Datapharm Australia, however, recommends the alternative option, which is for the overseas company to set up an affiliate company in Australia to be its legal entity. This legal entity must have at least one Australian director and an Australian address. Datapharm can introduce you to advisors who specialise in setting up legal entities for overseas sponsors and assist you with the set-up and maintenance of your local legal entity or company. The time to set-up the company, is less than a month (in fact has been done within a week). The advantage of this is that the cost to set-up the company is likely to be less than the added cost of a CRO providing this as a service.

INSURANCE

The new Australian company must be included in the overseas global company's clinical trial insurance certificate. The insurer can be an overseas entity.

CRO AS YOUR AGENT

The Australian CRO can act as the agent of the legal entity to do the majority of the trial documentation and management, and continue to liaise and connect the overseas sponsor with sites and the regulatory bodies. The local entity delegate will have a minimal role - usually to sign documents (ethics application, protocol, indemnity forms etc.) in the start-up phase. The local entity does not need to employ a project manager, medical monitor or receptionist – the Australian legal entities for some overseas sponsors function adequately in a serviced office setting.

Are There Any Advantages to the Sponsor Setting-Up a Legal Entity in Australia?

AUSTRALIA'S 43.5% R&D TAX INCENTIVE

You may not have heard the news – for some time now, many Australian biotechnology companies conducting clinical trials have benefitted from Australia's R&D Tax Incentive which is currently 43.5% (www.business.gov.au/assistance/research-and-development-tax-incentive).

Your Australian entity may benefit from this tax incentive. Eligibility for this incentive can be confirmed with our Consultant R&D Tax specialists. There is a requirement for the 'group turnover' to be less than $AUD 20M. The information in this document is general in nature and specific advice will be required to provide guidance on your company's entitlement. We will connect you with our preferred advisors.

Note that Datapharm Australia, as your Australian CRO, is an RSP (Registered Service Provider) for the R&D Tax Incentive which makes it easier for you to apply for the refund.

Are there any Other Cost Savings for Overseas Companies Conducting a Trial in Australia?

Exchange Rate

Currently*, there is a very favourable exchange rate for AUD-USD and AUD-Euro:

Expenditure	AUD	USD	Euro
Clinical Trial Cost estimate:	$AUD 1,000,000	$USD 764,982	€ 692,029
43.5% Tax Credit	$AUD 435,000		
Overall cost estimate	$AUD 565,000	$ USD 432,215	€ 390,996

*Assuming 1AUD is equivalent to ~0.76 USD (current at November 2016)

I.e. If the Australian sponsor spends $AUD 1,000,000 on clinical trials and receives back the 43.5% R&D tax credit, they have effectively only paid $AUD 565,000 ($USD 432,215)!!

Do you need to do an IND (Investigational New Drug) application if you conduct your First Clinical Trials in Australia?

No, there is no need to do an IND in order to conduct a clinical study in Australia.

You can be in the process of submitting an IND for future US or global studies, while the Australian studies are underway.

What are the Regulatory Processes for Clinical Trials in Australia?

In Australia, most clinical studies involving investigational products or devices, are reviewed by a HREC (Human Research Ethics Committee). Once approved by an HREC, a CTN form (Clinical Trial Notification) is sent to TGA using the new online submission format (www.tga.gov.au/form/ctn-scheme-forms). In the new method of submission, original signatures are no longer required, as the sponsor declares that the HREC has approved the study and that the trial will be conducted according to:

Guidelines for Good Clinical Practice (GCP): www.tga.gov.au/sites/default/files/ich13595an.pdf, and The "National Statement on the Ethical Conduct in Research Involving Humans" (published by the National Health and Medical Research Council): www.nhmrc.gov.au/_files_nhmrc/publications/attachments/e72_national_statement_may_2015_150514_a.pdf

In the case of Clinical studies that involve gene therapy or any study that may be considered by HREC of uncertain risk, you may need to submit a CTX (Clinical Trial Exemption) application to TGA. This involves preparing a hard copy application according to a particular format (www.tga.gov.au/form/ctx-scheme-forms) which is signed and submitted to TGA for review.

"The choice of which scheme (CTN or CTX) to follow lies firstly with the sponsor and then with the HREC. Studies in which medicines and medical devices that are already included on the Australian Register of Therapeutic Goods (ARTG) and are used within their approved indications and doses do not need to be subject to CTN or CTX requirements. However where they constitute research they will still need to be approved by an HREC."

[See TGA Guideline "Access to Unapproved Therapeutic Goods in Australia" and www.tga.gov.au/sites/default/files/access-hrec.pdf]
Most clinical studies in Australia are conducted under the CTN scheme with

only a small number reviewed each year as CTX. The HREC may request the CTX route if they have any concerns about the toxicology data or potential safety risks of the product under investigation.

Relevant questions about conduct of trials in Australia are answered on the TGA website (www.tga.gov.au/clinical-trials-faqs). The TGA also has a Clinical Trial handbook: www.tga.gov.au/publication/australian-clinical-trial-handbook .

What are the Regulatory Timelines in Australia?

Clinical trial projects generally require ethics approval through an NHMRC registered Human Research Ethics Committee (HREC) before proceeding with notification to Australia's regulatory authority, the Therapeutic Goods Administration (TGA). Clinics in the Private setting can receive a faster review from their HREC compared with Public Institution sites.

HREC: Private sites – Bellberry HREC has 5 committees and there are weekly meetings. If there are no changes requested approvals can be received in less than a month following HREC submission.

Public sites (e.g. hospitals): Apply to the Lead HREC using National Ethics Application Form (NEAF), or more recently updated to Human Research Ethics Application (HREA) Form. Public site HRECs meet less frequently – generally monthly. Once approved by a lead HREC, you will need to apply to other participating sites' RGOs (Research Governance Offices) using a SSA (Site Specific Assessment) Form. The latter can be a slower process however the Government is working on solutions to improve this time.

TGA: The TGA can take approx. one week to acknowledge the CTN in a letter that the trial can proceed. CTX has 30 or 50 day evaluation time.

Does each site need HREC approval?

Yes. Most private sites can submit to a Private HREC (Bellberry is commonly used) – advantage is that this HREC has five committees and can meet weekly so responses are swift. Public sites can submit to the Lead HREC with SSA to each site's RGO which is an extra layer of review.

What are the Fees for Clinical Trial Evaluation?

Regulatory TGA fees:

Prescription medicine clinical trial	Fee
Clinical trial notification (CTN)	$345
Clinical trial notification (CTN) - more than one trialling body	$345
Clinical trial exemption (CTX) - 30 day evaluation	$1,665
Clinical trial exemption (CTX) - 50 day evaluation	$20,800

What are the Ethics related Fees for Clinical Trial Evaluation?

Public Site: Hospital Institutional Fees can vary between institutions (contact us for examples)

HREC fees: Initial application with full industry sponsorship can be up to $5,500AUD

Additional Fee for Research Governance Office review fees: approx. $3740AUD

Private Site:

Bellberry HREC - Current Fees in AUD*

	Ex GST	Inc GST
Funded or Sponsored Studies		
New HREC Review Application (per site)	$5,500	$6,050
New Phase 1 HREC Review Application (per site)	$7,500	$8,250
Extension Study (per site)	$2,750	$3,025
Amendments (per site)	$550	$605
Investigator Brochure Updates (per submission)	$550	$605
Investigator-Initiated/Unfunded Studies		
New HREC Review Application (per site)	$2,750	$3,025
Extension Study (per site)	$1,375	$1,512.50
Amendments (per amendment, per site)	$275	$302.50
Multi-Centre Study Discount		
Site #1	$5,500	$6,050
Sites #2-5 (each)	$3,300	$3,630
Sites #6+ (each)	$2,300	$2,530

*As of 1 July 2016

GETTING STARTED

When Can You Import Investigational Product for Your Study?

Once you have the TGA CTN acknowledgement number for the first site, you can ship your drug into Australia.

Are There any Specific Labelling Requirements for Investigational Product in Australia?

Yes – Datapharm can advise on your product labels [See TGA document www.tga.gov.au/questions-answers-code-good-manufacturing-practice-medicinal-products Annexe 13].

Datapharm can also produce a randomisation list and code-break envelopes customised for your study. Alternatively, Datapharm provides online randomisation and dispensing from depots to sites globally using our eCRF system.

How does the Overseas Sponsor Locate Suitable Sites in Australia?

Datapharm will conduct a feasibility survey and provide a list of potential sites that are available to conduct studies in your therapeutic area. The most suitable are selected based on access to participant population and experience. Selected sites are qualified at a pre-study site visit.

Datapharm uses innovative methods in social media to improve subject recruitment. For example, a Datapharm initiative is australianclinicaltrials.com to showcase Australian investigational sites and assist sites with advertising their trials using social media. More investigational sites are joining this website. It is a great tool for overseas sponsors to do an initial feasibility for their studies in Australia.

What are some advantages for running clinical trials in Australia?

Seasonal studies: influenza, rhinitis, seasonal allergic conjunctivitis, asthma – Take advantage of reverse seasons to jump start your environmental studies. Your first pollen study can kick off in Australia in our spring (September) and be complete prior to your northern hemisphere study starting the next year!

Demographics: Australia's multicultural demographic allows for the inclusion of various racial backgrounds in studies. Some Asian bridging studies are conducted in Australia.

Some illnesses are more common: for example particular skin cancers for oncology studies as there is a high incidence of melanoma in Australia.

Does Australia have any Phase I sites?

Yes: The following four sites are well established and set-up with beds to conduct PK, bioequivalence, drug interactions and 'first in humans' studies. Phase I Units have databases of healthy volunteers, and some have additional capacity to conduct early phase studies in patient populations.

State	Location	Name
Queensland	Brisbane	QPharm
South Australia	Adelaide	CMax
Victoria	Melbourne	Nucleus Network
Western Australia	Perth	Linear

Furthermore, some oncology units conduct Phase 1 oncology studies.

Is Clinical Trial Data from Australia Accepted by Global Regulators (eg FDA, EMA)?

Yes: Australian clinical studies are conducted to international standards of ICH GCP, other disease specific guidelines (FDA and EMA) and clinical data is collected compliant with 21CFR Part 11 and CDISC standards. It is easy to integrate and publish your Australian clinical data for regulators as it is produced in an internationally recognised format.

Clinical Trials Research Agreement	CTRA	Templates available on Medicines Australia https://medicinesaustralia.com.au/policy/clinical-trials/clinical-trials-research-agreements/
National Ethics Application Form	NEAF	Currently being replaced by HREA
Human Research Ethics Application	HREA	See presentation on changes www.f1solutions.com.au/nhmrcs-webinar-on-hrea/
Patient Informed Consent Form	PICF	National PICF http://www.nationalpicf.com.au/
Indemnity Form		Standard and HREC review form and compensation guidelines on Medicines Australia https://medicinesaustralia.com.au/policy/clinical-trials/indemity-and-compensation-guidelines/

WHO IS DATAPHARM AUSTRALIA ?

- Australia's Original Full Service CRO
- 30 years experience in conducting Clinical Trials in Australia
- Australian owned and managed
- Worked in over 35 therapeutic areas Phase I to IV
- Flexible – responsive to needs of smaller biotechnology companies
- Friendly team – passionate about science and medical research
- Full service – from writing protocol to final study report
- Experts in web-enabled technology
- Uses social media to improve subject recruitment
- Registered Research Service Provider (RSP) with AusIndustry
- Established australianclinicaltrials.com to showcase Australian investigational sites and assist sites with advertising their trials

INTELLIGENT CLINICAL TRIALS DOWN UNDER

DatapharmAustralia

www.DatapharmAustralia.com

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