Down-under Wonders?

Clinical Trial Evolution in Australia & New Zealand

Gerard Dunne

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LAST TIME WE checked in with what was going on in Australia and New Zealand,[1] the ANZTPA combined regulatory process was hitting major hurdles, and was canned in mid-2007. So what's been happening since? Has it been growing like the rest of the Asia/Pacific region? Is it still a good place to do clinical research, and what type of clinical trials best suit the habitat?

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Growth

LET'S START WITH what's happening: "There are currently about 3700 trials on the Australian New Zealand Clinical Trials Registry, which listed an average of 90 new trials per month in 2009. This is a 'substantial increase' from a monthly average of 73 in 2008 and 54 in 2007. … Clinical trials are worth A$450 million a year" – Herald Sun, 14 February 2010.[2]

Hence, growth rates on the registry are 25%+ over the past two years, although some of this may be attributable to a greater awareness and use of the Australian New Zealand Clinical Trial Registry (ANZCTR) registration process.[3]

The table below, from Nature Reviews Drug Discovery,[4] shows the growth rates in clinical trials per region in the early part of previous decade (2002–2006). Already the trend can be seen of trials moving outside North America (admittedly from a very high base) and into other regions, as the number of trials as a whole has also grown tremendously over the period. While Oceania (defined here as New Zealand, Australia and Japan) did well, other areas such as Asia increased more rapidly (although from a much lower base for their populations).

Region	Change (2002-2006)
N America	-6.90%
W Europe	3.50%
Oceania	9.30%
L America	19.80%
Asia	20.40%
E Europe	24.00%

Table 1 Growth rates of clinical trials by region, from 2002 to 2006.3

Taken together with the more recent figures at the beginning of the article, an accelerating trend can be seen from the traditional centres of clinical research into new regions as discussed early last year in the New England Journal of Medicine.[5]

The general trend to globalisation, particularly amongst US companies looking outside North America, has been a large boon to phase 1 and 2 work undertaken in the Australasia region.

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Regional competition

People ask how the rise of India and China with their large populations, is affecting clinical trials in the region. While we expect these two, and others, to continue to grow rapidly in research, with their large scale and developing infrastructure, they are seen as more a destination for later phase research. Thus, there is little direct impact on the type or number of trials in the foreseeable future. New Zealand and Australia have usually contributed only a small portion of the patients to global phase 3 studies, unless it's been in an indication particularly prevalent in Australasia, and we would also expect this to continue to be the case.

Proof-of-concept trials

The big area of growth in the region has been early phase clinical trials, in particular proof-of-concept trials for North American and European companies. A higher proportion of studies are early phase (25%) than in any other region in the world.[4]

The reason is that biotechnology and medical device companies like the pragmatic environment for running trials. While they must be IND/IDE-ready in terms of pre-clinical data, they don't need to have an IND/IDE in order to do the trials in Australia or New Zealand. This makes the region an attractive option for companies to get proof-of-concept data and thus support for the next stage of their clinical development.

Medical device directive

As well as globalisation, some of the changes associated with the EU Directives have meant Western European companies have also looked abroad to run trials. The latest medical devices directive (2007/47/EC), which required compliance by March 21st 2010, may also have an impact for Australia and New Zealand.

For instance, its implementation in Germany (4th MPG) means that all but low risk devices will now require competent authority (BfArM) approval as well as ethics. In New Zealand, only ethics approval is required for medical device trials, which means overseas firms from start-ups to global top-10 companies may well look to do bench testing and run trials here.

Therapeutic areas

Melanoma, certain respiratory conditions, and some infectious diseases (eg, tropical diseases in northern Australia, hepatitis in northern New Zealand) are particular areas of research, along with the prevalence of

> *"Australia established standard Clinical Trial Research Agreements [in 2009], while New Zealand… is working on [one] for sites in 2010."*

'western' diseases, such as cardiovascular disease and diabetes.

Based on the past four years' data from the local ANZCTR register, for example, the three major therapeutic areas for trials in New Zealand are cardiovascular disease (12% of trials), respiratory disease (11%) and cancer (9%).

Australia is recognised as one of the most highly developed countries in which to do stem cell research, while New Zealand has been doing interesting work in xenotransplantation, in part as a result of its unique environment and lack of some zoonotic diseases found elsewhere.

New Zealand in particular is also seen as a good place in which to do medical device trials, as these can get started quickly and are cost-effective to do, again providing good rapid proof-of-concept data for device developers.

Regulatory & procedural changes

☐ WHILE THE COMBINED ANZTPA regulatory initiative is on hold, the drivers to harmonise both internally and with international standards have continued.

New Zealand's Good Clinical Research Practice interim guideline, similar to ICH-GCP, came up for review and consultation[6] last year and is shortly to be released. As the review stated, *"This will be the European Guideline (CPMP/ICH/135/95) with modifications as required to meet New Zealand-specific legal or ethics requirements"*.

Each country has also made moves to harmonise legal documents, eg indemnity and clinical trial agreements. Australia established standard Clinical Trial Research Agreements[7] last year, while New Zealand established a standard Indemnity Agreement[8] also in 2009, and is working on a standard Clinical Trial Agreement for sites in 2010.

Ethics committees

New Zealand has a single ethics committee review process for clinical trials regardless of the number and location of sites. When it was first established, it took a year or so for the process to bed down, but it now works well. A review of the process was undertaken in 2009 and some changes were made to streamline procedures, reflected in refinements to the National Application Form, a single form used throughout the country for ethics applications.

Australia is also looking at doing the same across the country, known as the HoMER initiative.[9] In the meantime, some of the Australian states have been moving towards a single process. The first to implement this has been New South Wales, where they have also experienced teething issues. Other states are watching in the hope of learning form this and implementing an expedited process.

At the same time, Australia has seen the growth of its first independent not-for-profit ethics committee, Bellberry, used by private clinics and GP practices that don't have an institutional committee. A second independent human research ethics committee was formed recently by the Queensland Clinical Trials Network (QCTN).

Site standards & accreditation

Similar to the UK and its UKCRC initiative, sites in Australia and New Zealand have been moving towards setting standards and accreditation. In Australia, the Victoria Managed Insurance Authority has published a set of SOPs online for sites, as has the Cancer Institute of New South Wales.

Part of the review of Good Clinical Research Practice in New Zealand is a proposal for the introduction of a process enabling applicants for approval of clinical trials to self-certify that the site(s) where the trial is to be conducted have appropriate facilities, staff and procedures to care adequately for trial subjects.

Sites already complete a locality assessment as part of the ethics approval process to take part in a clinical trial, and trends suggest more formal training and accreditation over time.

Clinical research profession

☐ THERE ARE A number of initiatives, similar to those in the UK & Ireland,[10] to establish career structures, training and development, for clinical research workers in the public health system and elsewhere.

There is a body of evidence to show that hospitals and clinics that are engaged in clinical research also offer a higher standard of clinical practice and patient care, for example from the American Medical Association (AMA).[11] Rather than clinical research being seen as an 'overhead' or a 'distraction' from clinical practice, it is

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ICR Events

As the title suggests this forum will cover MHRA inspections giving a general overview, a site perspective and there will also be an interactive session on preparing for an audit. Serious breaches will also be discussed.

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increasingly recognised as a vital adjuvant to good healthcare.

At the same time, there are an increasing number of clinical research events such as the NZ Association of Clinical Research conference, and in Australia CRX and TRX. There are also Post-Graduate Diploma courses in drug development at the University of New South Wales, and in clinical research starting in 2010 at Victoria University of Wellington, New Zealand.

Clinical trial inquiries

☐ BOTH GOVERNMENTS ARE currently running inquiries[12,13] into the state of clinical trials in their respective countries. They are keen to co-ordinate efforts, establish performance measures, streamline processes such as ethics approval, remove barriers and ensure patient access.

It's a sign that both countries are recognising the importance of clinical trials to their patient communities and to medical researchers and practitioners, in delivering better quality healthcare and outcomes for their citizens.

Conclusion

☐ NEW ZEALAND AND Australia are part of a much broader trend in the globalisation of clinical research, with sponsors no longer just looking in their own backyards to do trials, but instead looking around the world for the best regulatory regimes (reliable and quick) and best sites (reliable, quick and cost-effective) to do their trials.

With good medical infrastructure and high ratings for reliability,[14] both countries are well-suited for early phase clinical trials in particular, but will need to continue to up their game to stay ahead of the many other larger, developing jurisdictions breathing down their necks.

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