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## Clinical trials of medical devices: the changing scene

Improvements in communication and transportation technologies mean that the traditional locations for R&D are being challenged by up-and-coming sites. Here, Gerard Dunne, managing director of New Zealand-based contract research organisation BELTAS, lays out the advantages of conducting clinical trials in non-traditional countries

**T**raditionally, most medical device clinical trials have been run “close to home”. However, the definition of the terms “close” and “home” is changing rapidly; the device trial landscape is shifting.

Modern communications allow researchers to collaborate much more easily around the world. Not only are they able to find like-minded individuals – people with a similar interest in their field –

more easily, they are also able to exchange information quickly as they work towards a common goal. Thus, “close” is increasingly used to mean “closeness of interests”, rather than geographic proximity.

Similarly, the term “home” is no longer restricted to meaning the place where the technology or company originated. In the past, most initial development of medical devices has happened in North America and Europe. However, with other

countries now developing their strengths in medicine, engineering, economics and other areas, “home” for device development can occur all over the world. For example, at the recent AdvaMed conference in the US, the delegation from New Zealand included a variety of device companies working on everything from exoskeletons to physiological status monitoring (a technique used in the recent rescue of Chilean miners).

Of course Europe and North America still have the lion's share of device trials, but it is this very popularity which means that initiating new trials in those geographic regions – particularly as a start-up – can be difficult. Many other regions with high standards of healthcare, notably New Zealand and Australia, as well as other Asia Pacific countries, are able to do similar device trial work and have advantages over Europe and North America. They often have greater capacity for device trial work, they do not have so many competing trials, and the speed at which trial work is initiated is particularly advantageous with early phase proof-of-concept trials.

### **New Zealand and Australia**

Both countries have been running clinical trials for over 20 years, and their expertise has increased substantially over that time. In a 2005 Economist Intelligence Unit report, Australia was placed number one out of six key destinations to carry out clinical trials, beating the US, UK, Germany and several Asian countries.

There are currently about 3,700 trials on the Australian New Zealand Clinical Trials Registry. However, the main advantage of this region is not numbers – the combined population of both countries is just 27 million people – but speed, with small proof-of-concept trials typically completed within six months of a finalised protocol.

Both countries have pragmatic ethics and regulatory regimes, and these allow proof-of-concept device trials to get up and running quickly and achieve rapid data turnaround. This means a company could “kill it fast, kill it cheap” if a device fails to perform. If it does come through, the company would gain an early data set that can be used to obtain the next round of funding for device development in target markets.

In New Zealand, device trials do not have to gain regulatory approval. They just need to obtain the go-ahead from an ethics committee, which typically takes 6-8 weeks. Moreover, only one ethics committee approval is required regardless of how many sites in the country are involved in the trial.

Australia does its scientific review through its ethics committees and it only requires a notification process to the regulatory authority before you initiate your trial. Again, the time it takes to initiate a trial is 6-8 weeks.

In a nutshell, the device should be IDE-ready, but an IDE is not required to conduct the trial.

### **Sponsor companies**

Another advantage that Australia and New Zealand have is their community of global key opinion leaders in areas including cardiovascular disease, diabetes and orthopaedics. For example, a considerable amount of bench testing of stents is undertaken in Auckland, New Zealand by John Ormiston, a world-leading investigator.

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Many offshore start-ups look to New Zealand and Australia to find investigators interested in their field, and who are willing to assist with proof-of-concept trials and contribute their trial experience to the device's development. Because the countries are a manageable size and have a known number of quality sites, an assessment can be made fairly quickly as to whether a device is ready and able to undergo clinical trials in the region.

Below is a case study illustrating the process for a US company initiating clinical trials in New Zealand.

### **Case study**

A US cardiovascular device company approached New Zealand's Auckland Hospital looking to run initial human clinical trials with their device. The principal investigator discussed the design of the trial with the company's staff and agreed to recruit an initial five subjects. The trial was approved by the ethics committee and several of the company's team flew in to instruct physicians at the site in the procedure, and oversee the first cases. These were done in a couple of tranches and the data remitted to the company. The whole procedure, from the company first approaching the hospital, to the first data being remitted to the company, took around six months. Pleased with the results, the company initiated a further trial at the hospital.

This is not an uncommon outcome. On one hand, it reflects how one of the main hurdles for North American and European device companies is getting over the

concept of running their trials at a distance. Conversely, once they have successfully run one trial in the region, they come back again and again; the repeat rate for client studies runs at between 80 and 90%.

### **Limitations**

One key limitation of doing your clinical trials in Australia and New Zealand is the size of its population. With just 27 million people, trials are typically of the order of 25-250 subjects (with some exceptions). Thus, companies that carry out device and diagnostic trials in these countries would typically be looking for rapid proof-of-concept data for investors. They may come back and do several trials as they improve the device, before going for the IDE or CE mark. Safety, of course, is paramount and the ethics committees will want to see preclinical data in animals, depending on the device.

Once proof-of-concept is achieved, devices are typically trialled in their target markets with larger populations, although at times, Australia and New Zealand will be included in these trials as well, as part of a global study. Certainly many of the top 10 device companies include both countries in their ongoing global trials.

### **Other regions**

A number of countries in the Asia Pacific region have woken up to the opportunities for their patient populations and medical staff in having access to clinical trials and are also doing what they can to remove barriers. Such competition, where moderated by maintaining high standards as well as a pragmatic approach, should assist the future globalisation of device and diagnostic trials.

The rise of India and China with their large populations is likely to affect clinical trials in the region. While these two countries, and others, are expected 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 late phase studies, unless it's been in an indication particularly prevalent in the region, and this is expected to continue to be the case. So, these two countries are aiming to remain at the forefront of rapid, quality early phase proof-of-concept trials, while other Asia Pacific countries develop into large later phase trial and market destinations for products as they move beyond this stage.